CALCIUM-LOADING TEST AND BONE DISEASE IN PATIENTS WITH UROLITHIASIS

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Summary

A group of 121 patients with a history of multiple or complicated calcium urolithiasis were divided into three subgroups: normal, absorptive and renal/resorptive calciuria by means of a calcium-loading test. Patients with renal hypercalciuria had lower bone mineral content (BMC) than the other groups but did not differ in amount of bone or TmPO4/GFR. The 24-hour urine calcium excretion was elevated in patients with renal and absorptive type of hypercalciuria but not in patients with normal calcium-loading test and there was no correlation to BMC. The c-AMP/creatinine seemed to discriminate patients with resorptive calciuria from patients with renal calciuria. It is suggested that only patients with renal hypercalciuria should be treated with calcium-retaining drugs such as thiazides.

Introduction

There are conflicting opinions in the literature regarding the value of differentiating hypercalciuria into subgroups [1, 2]. The present study attempts to clarify this subject and especially the relationship to bone metabolism in the subgroups.

Patients and methods

During 1977–1981, 121 patients with calcium urolithiasis were studied in our hospital. There were 34 women and 87 men, aged 20–60 years, with a serum creatinine less than 150μmol/L. Thirteen patients had multiple stones but had never been operated, whereas 108 patients had been operated for urolithiasis one or more times. Sixty patients had a family history of urolithiasis.
A calcium-loading test according to Pak [3] was performed in all.

During the following days, 2 x 24-hour urine collections were obtained for determination of calcium, phosphate and creatinine with the patients on a normal diet. The renal phosphate threshold was calculated as TMPDPO4/GFR [4]. The bone mineral content (BMC) was measured on the distal forearm using a photon absorption technique [5]. The quantity of bone was estimated from the Barnett-Nordin [6] and the Exton-Smith [7] indices (D-d/D and D^2-d^2/D-L, where D = external diameter of bone, d = internal diameter, L = length of bone), both on X-ray pictures of 2nd metacarpal bones and on photon-absorption curves of radius and ulna of both arms. Cyclic AMP (cAMP) was determined with a protein binding assay and parathyroid hormone (PTH) with a radioimmunoassay with antiserum directed mainly against the C-terminal part of the hormone. The results of the urine analyses, the renal phosphate threshold and the photon absorption studies were compared with values in 114 normal controls, randomly chosen from the general population in our region. As TMPDPO4/GFR and BMC were influenced by age we used the unit standard deviation, SD, for comparisons with the patients.

Results

The calcium-loading test separated the patients into three groups: those with normal calciuria (38%), with absorptive calciuria (25%) and with renal/resorptive calciuria (37%) (Figure 1). There were no clear differences in the urinary cAMP/creatinine ratio or serum PTH between the groups but the fasting urinary cAMP/creatinine (before calcium-loading) correlated positively with the fasting urinary calcium/creatinine ratio, signifying that patients with more severe renal calciuria were more parathyroid stimulated. Five patients with primary hyperparathyroidism were all in the renal/resorptive group of calciuria and the cAMP/creatinine, which was elevated or in the upper normal range before the load, was clearly elevated after the calcium load (Figure 1). The 24-hour urinary calcium/creatinine ratio was elevated in the absorptive and renal/resorptive group of patients but not in patients with normal calcium-loading test when compared to normal controls (Figure 2). The BMC was lower in patients with renal/resorptive calciuria compared to the other groups (Figure 3) and the BMC correlated negatively with the fasting urinary calcium/creatinine ratio (Figure 4). However, there were no deviations in BMC from normal controls, when all patients were taken together, and there was no correlation between the 24-hour urinary calcium and the BMC, nor within any separate group of calciuria.

The TMPDPO4/GFR was not different from age-matched controls, and there was no difference between the groups. Only the five patients with hyperparathyroidism had lower values. Furthermore there was no correlation between TMPDPO4/GFR and BMC or the parameters of bone quantity. The amount of bone evaluated as Exton-Smith index on the photon absorption curves was significantly lower in the total patient group than in the normal controls, but there were no differences between the separate groups of calciuria.
Figure 1. Groups of calciuria before and after calcium-loading test in 121 patients with calcium urolithiasis. Patients with primary hyperparathyroidism (resorptive) are denoted as open circles (○). Urinary calcium/creatinine is given in mg/mg and urinary cAMP/creatinine in µmol/gram creatinine. The horizontal lines indicate ± 2 SD in normal controls.
Figure 2. 24-hour urinary calcium/creatinine in normal controls and different groups of calciuria

Figure 3. BMC in different groups of calciuria
Discussion

The main advantage of dividing patients with calcium urolithiasis into groups with absorptive, renal, resorptive and no hypercalciuria is to provide a basis for ‘selective’ treatment [1]. Patients with resorptive calciuria, i.e. patients with primary hyperparathyroidism should in most cases be subjected to parathyroid exploration. However, it is also evident that stone-formers with hypercalciuria, elevated serum PTH and perhaps other signs of secondary hyperparathyroidism and renal calciuria, should not be parathyroidectomised. In this study it could be shown that patients with renal calciuria had lower mineral content, BMC, than other groups of calciuria, although the difference was not as great as that reported by Pak [1] or earlier by us [8]. As to the bone metabolism it seems logical to treat this group of patients with calcium-retaining drugs such as thiazides, although no randomised study proving its effect has so far been published. To treat the absorptive group with thiazides seems dubious as the BMC then may increase above normal [1] and as thiazides may even be nephrotoxic [9]. The described bone disorder in this study is rather a mineral loss than a loss of bone quantity, since there were no differences in the Exton-Smith indices between the groups. The bone quantity in the whole group of patients was, however, lower than in normal controls.

A phosphate leak as a cause of the bone disorder, as suggested by Bordier et al [10], is unlikely as the TmPO4/GFR was not different from normal controls in any group of patients and showed no correlation with BMC or bone quantity parameters.
References

2. Peacock M. *Contrib Nephrol* 1982; 33: 152