RENAL STONE FORMATION IN PRIMARY HYPERPARATHYROIDISM - ROLE OF TUBULAR DYSFUNCTION

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The formation of calcium stones is perhaps the best recognized feature of primary hyperparathyroidism (HPT). Its frequency in different clinical series varies from 25% - 50%, the lowest figure being obtained in the most recent studies, where HPT was detected fortuitously during health screening studies. The mechanism for the markedly increased propensity for stones in HPT are not entirely clarified. For obvious reasons most interest has been directed to investigations of calcium metabolism but although HPT patients with stones have a higher mean urinary calcium than the stone-free individuals¹, hypercalciuria alone can not explain why some, but not all, HPT patients form stones.

Parathyroid hormone (PTH) promotes bicarbonate excretion by interfering with its reabsorption in the proximal tubules and excess secretion of PTH can therefore give rise to a picture of proximal renal tubular acidosis (RTA)². It has also been claimed that a selective urinary excretion of low molecular weight (LMW) proteins ("tubular proteinuria") can be present in HPT and be reversible during the months following parathyroidectomy. Among consecutive normocalcemic, euparathyroid, patients with recurrent renal stones we³ have previously found evidence of tubular dysfunction in more than 20%. Most of these had incomplete types of RTA but also tubular proteinuria was a common finding.

In the present study we have applied these tests to tubular function in a series of patients in order to evaluate the frequency of tubular dysfunctions and its relationship to stone formation in HPT.
PATIENTS AND METHODS

Altogether 64 patients (13 males, 51 females) with a mean age of 62 years (range 25–81 years) were studied. They were consecutively admitted cases of hypercalcemia who subsequently were proven to have HPT after neck exploration. Pre-operative evaluation was performed shortly before surgery whereas the post-operative studies were carried out not earlier than three months after the operation.

The urinary excretion of β2-microglobulin was determined as an index of LMW-proteinuria by a radioimmunoassay technique (Phadebas, Pharmacia, Uppsala) in 2 h specimens obtained in the morning both before and after an intravenous calcium infusion test. The 24 h citrate excretion was measured by a citrate lyase method (normal range 1–5 mmol/24h). In 24 of the patients an ammonium chloride loading test was performed.

RESULTS

Out of the 64 patients in this study 29 had a history of stones. The stone-forming patients had a higher mean urinary calcium than the stone-free cases but there were no other differences in the serum or urinary electrolytes (see Table 1). In all the patients a pre-operatively raised serum concentration of PTH was normalized post-operatively and urinary calcium also decreased in every patient.

The urinary citrate excretion was of the same magnitude in the two groups of patients. A slight reduction was evident during the first postoperative period. The urinary excretion of β2-microglobulin was raised in 12 patients (4 with stones). The excretion was not affected by calcium infusion and a raised output persisted also after parathyroid surgery.

Among the 24 patients, where the renal acidifying capacity was studied all had a normal basal acid-base status. During ammonium chloride loading one of them could not produce an acid urine despite systemic acidosis (distal RTA). One of the others had increased losses of bicarbonate and thus presented a picture of proximal RTA. The defective acidifying capacity persisted postoperatively.

DISCUSSION

In this series of consecutive patients with surgically proven HPT impaired acidifying capacity was a rare finding, and in the two cases where an incomplete defect was found it persisted also after correction of parathyroid hyperfunction. Although exogenous PTH will cause bicarbonate wasting and induce acidosis, it appears that in patients with mild-to-moderate HPT effects on the acidifying ability will not explain the increased propensity for stone formation.