The Role of Calcitonin in Calcium Stone Formation

R. Shainkin-Kestenbaum
Y. Winikoff
E. Paran
L. Lismer

Departments of Nephrology and Urology, Soroka University Hospital, Beersheva, Israel

Urinary calculi represent a common world-wide disorder, the frequency of occurrence varies from country to country. In the Middle East, including the southern arid regions of Israel, renal stones are very common [1]. It has been suggested that stone formation is due to an imbalance between urine saturation and inhibitory activity [2]. A number of risk factors have been identified. These include family history, dehydration, urinary pH, diet, hyperoxaluria, hyperuricosuria, medications, hyper-parathyroidism, elevated plasma levels of 1,25-(OH)2D3 and hypercalcuria [3, 4]. However, even a patient with multiple risk factors does not necessarily develop renal stones.

The physiological importance of many factors regulating calcium metabolism in renal stone formation such as PTH and 1,25-(OH)2D3 have been studied extensively [5–7]. However, surprisingly, no comprehensive data are available on the possible involvement of calcitonin which is a hypercalcuric and hyperphosphaturic hormone [8,9]. High levels of calcitonin were detected by us in patients with idiopathic hypercalcuria [10, 11]. Persistent hypercalcuria increases the risk of crystalluria so that studying calcitonin levels in calcium-stone forming patients may add to a better understanding of the endocrinological basis of calcium nephrolithiasis.

The problem of calcitonin’s effect on the kidney is complicated by the presence of up to 5 molecular forms [12]. Most calcitonin is metabolized in the kidney [13], and plasma concentration is increased in renal failure [14], but its actual pathophysiologic role in renal osteodystrophy is still conjectural.

The evidence of the role of calcitonin in renal stone formation is sparse. In children with idiopathic hypercalcuria, there was a significant increase in plasma calcitonin levels [11,15]. In unpublished studies on 27 patients with bilateral, multiple or recurrent calcium nephrolithiasis with normal renal function, it was found that only 2/27 (7%) had normal plasma calcitonin levels. 2 (7%) had technically abnormal calcitonin. 11 patients (41%), 5 males and 6 females had calcitonin levels significantly lower than normal (0.05 ± 0.01 ng/ml vs. normal range in our laboratory of 0.1–0.2 ng/ml). 5 of these patients had calcium oxalate stones; 3 had calcium phosphate stones. On the other hand, 12 patients (44%) had plasma calcitonin levels which were higher than normal (0.35 ± 0.03 ng/ml vs. normal range of 0.1–0.2 ng/ml). Plasma calcium and phosphorous levels were normal but plasma PTH values were in the normal range in only half of the patients. Furthermore there was a significant difference in that PTH levels were lower in the group with the lower calcitonin values, than in
the group with the higher calcitonin values. The latter group had 6 calcium oxalate stones positively identified in it. Plasma uric acid levels in both groups were at the upper limit of normal.

What is the value of these observations, other than as a collection of nonrelated facts? Let us construct a hypothesis. Hypercalcitoninemia causes hypercalcuria and hyperphosphaturia. This alone is sufficient to increase urine calcium concentration and in the presence of adequate urinary concentrations of oxalate or phosphate, calcium oxalate or phosphate stones may form. The effect of calcitonin on stone formation inhibitors is unknown, as is the effect of calcitonin on oxalate metabolism. The renal calcium load in hypercalcitoninemia may come from extracellular fluid calcium. Unlike PTH, calcitonin prevents calcium from leaving bone [16]. On the other hand, low plasma calcitonin levels may effect bone remodelling and mineral homeostasis by permitting increased calcium loss from bone into extracellular fluid and thus furnish an increased amount of calcium for potential excretion into the urine.

Clearly, we need to know more about calcitonin in the various types of renal stone and the effect of calcitonin on oxalate and urate metabolism, but meanwhile, we should

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include disturbances of calcitonin metabolism as one of the possible disorders suspected to be associated with calcium stone formation.

References