Mineral Content of Human Skin in Uraemia—Effect of Secondary Hyperparathyroidism and Haemodialysis

SHAUL G MASSRY, JACK W COBURN, DAVID L HARTENBOWER, JAMES H SHINABERGER JOHN R DEPALMA, ELEANOR CHAPMAN and CHARLES R KLEEMAN

Cedars-Sinai Medical Center, Los Angeles Veterans Administration Center and Department of Medicine, UCLA School of Medicine, Los Angeles, California, USA

Radiographic evidence of soft tissue calcification is not infrequently seen in patients with chronic renal failure (Hubbard & Wentworth, 1921; Smyth & Goldman, 1934; Bogdonoff et al, 1956; Katz et al, 1969; and Massry et al, 1969). However, it is likely that calcium may accumulate in soft tissue long before it becomes apparent by x-ray. The present study was undertaken to determine whether chemical analysis of soft tissue might be useful in the early detection of soft tissue calcification and to evaluate some of the factors that predispose to an increase in the calcium content of soft tissues in the uraemic patient.

MATERIAL AND METHOD

Samples of skin, weighing 100 to 300 mg, were obtained either by elective biopsies or during various surgical procedures from normal subjects and from patients with advanced chronic renal failure, with or without evidence of clinically overt secondary hyperparathyroidism. The group with renal disease included those managed conservatively without need for dialysis and others who were maintained by regular haemodialysis for periods of 2 to 50 months. The criteria used to distinguish patients with clinically overt secondary hyperparathyroidism were those previously reported from this laboratory (Massry et al, 1969). In ten patients, the calcium content of skin was evaluated before and one to ten months after subtotal parathyroidectomy. The effects of using different dialysate concentrations of calcium (6.0 mg/100 ml and 8.0 mg/100 ml) and magnesium (0.6 mg/100 ml and 1.8 mg/100 ml) on the calcium and magnesium content of skin were also evaluated. Skin samples were scraped free of fat, blotted, minced and divided into two or three pre-weighted tubes for duplicate or triplicate analysis. Details of the method for the chemical analysis of soft tissue have previously been reported (Bradbury et al, 1968).
RESULTS

Figure 1 depicts the individual values for the content of calcium in the skin of normal subjects and patients with chronic renal failure. The calcium content of the skin in 17 normal subjects ranged between 231 to 432 mg/kg dry weight (323 ± 13, mean ± se). The uraemic patients with clinically overt secondary hyperparathyroidism, whether treated with haemodialysis or not, had amounts of calcium in their skin which were significantly elevated to 488 ± 29 and 554 ± 41 mg/kg dry weight, respectively. In the absence of the syndrome of clinically overt secondary hyperparathyroidism, the calcium content of skin was usually within the normal range. The calcium content of the skin of the patients with renal failure did not correlate with the level of serum calcium, the product of the blood concentrations of calcium and phosphorus, or the duration of haemodialysis.

Following subtotal parathyroidectomy for clinically overt secondary hyperparathyroidism in ten patients, the calcium content of the skin fell by 119 ± 34 mg/kg dry weight. There was considerable variation in the decrease of calcium in the skin from one patient to another; and skin calcium failed to change in two patients (Figure 2).
When patients, who did not have evidence for clinically overt secondary hyperparathyroidism, were treated with haemodialysis using dialysate containing 8.0 mg of calcium per 100 ml for 2 to 12 months, there was a significant increase in the calcium content of their skin. However, radiographic evidence for soft tissue calcification did not appear in these patients during this period of time. In patients treated for periods of several months, first with a dialysate containing calcium in a concentration of 6.0 mg/100 ml and then with a dialysate containing 8.0 mg of calcium per 100 ml, the calcium content of skin was 355 ± 11 and 510 ± 61 mg/kg dry weight respectively (p < .01).

The magnesium content of the skin in patients undergoing maintenance haemodialysis is also affected by the concentration of magnesium in the dialysate. In Figure 3, the mean values of the magnesium content of skin in two populations of patients treated with haemodialysis for periods of two
months to five years with dialysates containing magnesium in concentrations of either 1.8 or 0.6 mg/100 ml are compared. Although there was an overlap between the individual values, the skin content of magnesium is significantly different (p < .01) between the two groups.

**DISCUSSION**

The results of the present investigation demonstrate that an increase in the calcium content of skin can be detected by the chemical analysis of small samples of skin, which can be easily obtained by biopsy. This study does not prove that the amount of calcium in the skin is an index of the calcium content of certain vital soft tissues. Other organs, such as lung, kidney and stomach, which display changes in local pH, may have a greater predilection for calcium deposition. It is likely that conditions which cause an increase in the calcium content of the skin may also enhance calcium deposition in other organs.

This study also demonstrates that the calcium content of skin from patients with renal failure and clinically overt secondary hyperparathyroidism
is higher than that of normal subjects and of uraemic patients without this syndrome. The decrease in the amount of calcium in the skin after subtotal parathyroidectomy further suggests a relationship between the deposition of calcium in soft tissues and the activity of the parathyroid glands in patients with renal failure. Twenty-six of the patients who had high calcium levels in their skin, had also x-ray signs of osteitis fibrosa while 20 patients had radiographic evidence of soft tissue calcification. This observation suggests that with progressive bone resorption produced by high blood levels of parathyroid hormone found in such patients, calcium is released into extracellular fluid and is then deposited into soft tissues; the increase in calcium could, therefore, be detected by the chemical analysis of such tissues. Only when the magnitude of soft tissue calcification increases greatly will calcium deposition become radiographically evident.

The present investigation also demonstrates that the use of a dialysate with a calcium concentration of 8.0 mg/100 ml causes a significant increase in the calcium content of the skin. This observation suggests that this concentration of calcium in dialysate may eventually produce or aggravate clinically significant soft tissue calcification.

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