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Bone Mineral Content in Systemic Sclerosis Measured by Photonabsorptiometry

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Abstract. The bone mineral content of the radius in 37 patients with systemic sclerosis was measured with Americium^{241} photon absorptiometry. The content was found reduced ($p<0.05$) in patients with systemic sclerosis compared with a group of healthy controls matched for age and sex. Analyses of calcium 'total', calcium ion, phosphate and the parathyroid hormone level in the serum, and the excretion of calcium and phosphate in the urine all proved normal. It is discussed whether the reduced bone mineral content in systemic sclerosis may be an effect of the immobilization of the hands affected by the disease.

Collagen is quantitatively the most important product of the osteoblast, and an important component of the organic bone matrix. The subsequent mineralization occurs on the surface of the collagen fibrils (2).

Collagen of the skin and collagen of the bone belong to the same immunological type.

Systemic sclerosis is characterized by an abnormal production of collagen, and calcifications of the skin in the form of hydroxyapatite are seen in about 20% of the patients (3). Cultured skin fibroblasts from patients with systemic sclerosis show increased accumulation of calcium (1).

Previous studies on the bone mineral content in patients with systemic sclerosis have been performed using only radiological techniques (6). In the present study, the mineral content of the forearm bones in a group of patients with systemic sclerosis was measured quantitatively by photon absorptiometry. The results were correlated to the clinical status and to laboratory parameters of mineral metabolism.

MATERIAL AND METHODS

Patients with a diagnosis of systemic sclerosis treated at the Department of Dermatology, Rigshospital, were selected according to the following criteria:

1. diagnostic criteria fulfilling the demands of the American Rheumatism Association,
2. duration of the disease ⩾3 years,
3. age below 70 years,
4. no hormonal therapy (including corticosteroids),
5. no known endocrine diseases,
6. no previous fractures of the distal radius.

Of 45 patients, 37 met these criteria, 30 women and 7 men. Their mean age was 55.7 years (range 20–69) and the mean duration of systemic sclerosis was 8.9 years (range 3–13). Twenty-eight patients received treatment with penicillamine combined with glutamine. Nine patients received treatment for systemic sclerosis with other drugs (glutamine, hydralazine, phenytoin).

The bone mineral content (BMC) of the radius was measured by Americium^{241} photon absorptiometry. A standardized part of the distal radius of the right arm, 5–10 cm from the end, was selected for the determination according to the method described by Søren Madsen et al. (4).

Serum concentrations of total calcium, ionized calcium, and of phosphate were determined by routine laboratory techniques. Parathyroid hormone levels were determined at Medicinsk Laboratorium A/S, Copenhagen, by radioimmunoassay.

Radiological examination of both hands was performed to diagnose calcifications of the soft tissues.

Frequencies were compared assuming a Poisson distribution, mean values by Student's *t*-test, and correlations were performed by the method of least squares. Probability values below 0.05 were considered statistically significant.

Table I. *Calcium and phosphate analyses of serum (S) and urine (U) in 37 patients with systemic sclerosis*

		Systemic sclerosis, $n=37$ Mean (range)	Normal range
S-Calcium 'total'	mmol/l	2.34 (2.27–2.67)	2.20–2.60
S-Calcium 'ionized'	mmol/l	1.19 (1.01–1.29)	1.15–1.35
S-Phosphate	mmol/l	1.15 (0.86–1.42)	0.80–1.50
S-Parathyroid hormone	µg/l	0.44 (0.28–0.65)	0.22–0.50
U-Calcium	mmol/24 h	2.90 (0.90–6.30)	2.00–8.00
U-Phosphate	mmol/24 h	14.50 (3.50–40.00)	10.00–45.00

RESULTS

BMC was reduced in 9 women and 1 man, i.e. less than the mean −1 SD of a control group matched for sex and age ($p<0.05$, Fig. 1).

Twenty patients (19 women, 1 man) had soft tissue calcifications of the hands at radiological examination. Soft tissue calcifications were significantly more frequent in patients with a reduced BMC ($p<0.05$), and they were more frequent in women vis-à-vis men ($p<0.05$).

The results of the analyses of blood and urine are shown in Table I. There were no correlations between these parameters of mineral metabolism and BMC. The mean values of the parameters measured were within the normal ranges.

A reduced BMC was not significantly correlated to the duration of systemic sclerosis, but a tendency to decreasing BMC with increasing duration of the disease was noted.

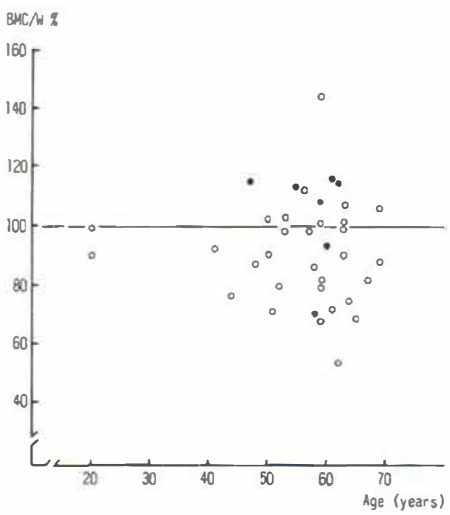

Fig. 1. Bone mineral content (BMC/W – g/cm²) of the distal part of the radius in patients with systemic sclerosis. Each value is expressed as a percentage of the mean of a control group matched for age and sex. Women = ○; men = ●.

DISCUSSION

Because of similarities between skin and bone collagen, increased BMC might be expected in systemic sclerosis. Yet we found reduced BMC. Radiological examinations of the skeleton have also shown osteoporosis (6).

Obviously, patients with acrosclerosis and contractures of the fingers do not have the normal physical mobility of their hands and thereby run an increased risk of osteoporosis. In this material of 37 patients, 28 had registered contractures of the fingers. The reduced bone mineral content of the radius in systemic sclerosis might therefore be attributed to the disability of the hand.

The effect of age on the BMC values was excluded in this study, since relative values, related to a control group matched for sex and age in each case, were used.

The reduced BMC was not an effect of involvement of the parathyroid glands by the disease resulting in hypoparathyroidism, since the serum calcium concentration, both total and ionized, and mean urinary excretion of calcium, were normal. Furthermore, the serum concentration of parathyroid hormone was normal. A normal calcium metabolism in patients with systemic sclerosis has also been found in a previous study (5).

A relation between reduced BMC and soft tissue calcification was found. If patients with soft tissue calcifications are less mobile, the relation could be explained as an effect of immobilization.

In conclusion, a reduced bone mineral content was found in patients with systemic sclerosis, but major abnormalities in the calcium metabolism could not be demonstrated.

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Irritation and Staining by Dithranol (Anthralin) and Related Compounds III. Cumulative Irritancy and Staining during Repeated Chamber Testing

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Abstract. Irritation and staining, the side effects of dithranol and related compounds have previously been studied after a single chamber-exposure. To mimic the therapeutic situation, the chamber application was repeated for 3 weeks on the uninvolved back skin of 17 psoriasis patients. In equimolar concentrations corresponding to 0.05% dithranol, dithranol caused markedly more erythema and staining than 10-propionyl dithranol and 10-butyryl dithranol, whereas 10-butyryl dithranol irritated and stained less than 10-propionyl dithranol. To reach the irritation and staining level of dithranol, a 4-fold higher concentration of 10-butyryl dithranol was required. During the first week the irritation culminated, declining later despite repeated applications, possibly because of exhaustion of anthrone-induced inflammatory mediators.

Key words: Psoriasis; Dithranol; Anthralin; 10-propionyl dithranol; 10-butyryl dithranol; Irritation; Staining; Repeated chamber testing

In previous papers (4, 5, 6, 7), skin irritation and staining caused by a single exposure of dithranol and some related anthrones was studied by applying the chamber-testing technique of Pirilä (8). In uninvolved skin of psoriasis patients the Irritant Dosis 50 (ID_{50}) as mmol/kg of petrolatum for dithranol, 10-acetyl dithranol, 10-propionyl dithranol and 10-butyryl dithranol were 0.2, 0.5, 1.5 and 4.5, respecitively (6, 7). A single exposure of irritating and staining anthrones does not mimic the therapeutic situation as well as repeated applications, and therefore the cumulative irritancy and staining of uninvolved skin of psoriasis patients was studied.

MATERIALS AND METHODS

17 hospitalized psoriasis patients volunteered for this study. In addition to dithranol, 10-propionyl dithranol and 10-butyryl dithranol were applied on the uninvolved back skin using 12 mm Finn chambers (8). The application was repeated every second day on exactly the same sites. In 9 patients the concentration used was 2 mmol/kg of white petrolatum for all three anthrones, and in 8 patients the concentration of dithranol was 2 mmol/kg, and those for 10-propionyl dithranol and 10-butyryl dithranol were 4 and 8 mmol/kg, respectively. In all patients the vehicle, white petrolatum, was estimated at every application. The reading scales were the same as before (4).

RESULTS

Fig. 1 shows the average alternate day alterations in erythema and staining in the group of 9 patients tested by the 2 mmol/kg concentration of dithranol (D), 10-propionyl dithranol (PD) and 10-butyryl dithranol (BD). There was no evidence of irritation or staining at the control sites tested with the vehicle white petrolatum. In the equimolar concentration of 2 mmol/kg D caused markedly more erythema and staining than PD and BD, and BD irritated and stained less than PD. During the first week of repeated testing the irritation reached the highest intensity: 2.7 for D, 1.3 for PD and 1.0 for BD. Later, despite repeated applications, the irritation declined, the average erythema value of the 20th day being 0.8, 0.6 and 0.3 for D, PD and BD, respectively. For D the staining was most intense during the second week (average value 2.5) and later decreased a little because of peeling. For PD and BD the staining value of 1.1 was reached during the third week.

Fig. 2 illustrates the average alternate day alterations in erythema and staining in the group of 8 patients tested with 2 mmol/kg of D, 4 mmol/kg