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BONE MINERAL CONTENT IN HYPERTHYROID PATIENTS AFTER COMBINED MEDICAL AND SURGICAL TREATMENT

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Excess of thyroid hormone(s) causes mobilization of bone mineral (MOSEKILDE & CHRISTENSEN 1977) and a negative calcium balance (COOK et coll. 1959). Roentgen ray and γ-ray densitometric measurements have shown a decreased bone mineral content in untreated hyperthyroidism (FRASER et coll. 1971, MEEMA & MEEMA 1972, SMITH et coll. 1973) and morphometric analysis of iliac crest biopsies have demonstrated an increased bone resorption and a decrease in the amount of both trabecular and cortical bone (MEUNIER et coll. 1972, MOSEKILDE et coll. 1977). The decreased amount of bone will cause a reduction of the compression strength and spontaneous fractures may be the consequence (NIELSEN 1952, RYCKEWAERT et coll. 1968, MEUNIER et coll.).

The aim of the present investigation was to elucidate to what extent the low amount of bone compared to that in normal controls could be detected by photon absorptiometry of the forearm, and also whether the bone mineral content and the bone mineral concentration increased after treatment of the hyperthyroidism, in order to evaluate whether these individuals represent a risk group for spontaneous fractures in the future.

Supported by the Danish Medical Research Council (No. 512-6673). Submitted for publication 23 February 1978.

Table 1

Chemical quantities of calcium-phosphorus metabolism in hyperthyroid patients and in normal controls

		S-calcium corrected (mmol/l)	S-phosphorus (mmol/l)	S-alkaline phosphatase (u/l)	U-calcium*	U-phosphorus**
Normal controls	Mean	2.508	1.18	147	430	1 965
	SE (N)	0.006 (160)	0.02 (60)	4 (60)	13 (60)	45 (60)
Hyperthyroid patients	Mean	2.662	1.19	225	815	3 121
	SE (N)	0.023 (20)	0.03 (20)	16 (20)	87 (20)	278 (20)
	p	<0.001	n.s.	<0.001	<0.001	<0.001

* calculated as (dU/calcium(mol)/dU-creatinine(mol)) × 10^3

** calculated as (dU-phosphorus(mol)/dU-creatinine(mol)) × 10^3

Material and Methods

The material comprised the following groups:

Group I: 20 untreated consecutively admitted hyperthyroid patients aged 28 to 69 years (mean 44.6). The diagnosis was based on symptoms and signs, determinations of total serum thyroxine ($S-T_4$, Tetralute ^{125}I Reagent kit, Ames), serum triiodothyronine uptake test ($S-T_4$-test, the Radiochemical Centre, Amersham) and the absolute ^{132}I uptake of the thyroid.

Group II: 33 individuals aged 28 to 68 years (mean 49.5) examined 1 to 16 years (mean 7.6) after combined medical and surgical treatment for hyperthyroidism. All were euthyroid, but 3 received substitution therapy with levo-thyroxine. All had normal serum concentrations of calcium and creatinine and none was immobilized.

Group III: Controls for group I and II selected from a normal series of 214 individuals of similar age and sex.

In the hyperthyroid group, fasting serum concentrations of calcium, phosphorus and alkaline phosphatase were measured by standard laboratory methods and the mean of measurements from three different days was calculated. The serum concentration of total calcium (S-calcium, mmol/l) was corrected for individual variations in the serum albumin concentration (S-albumin, mmol/l) according to the formula: S-calcium, corrected = 1.2 (0.700 − S-albumin) + S-calcium. This formula was derived from the regression equation of S-calcium on S-albumin in 160 normal individuals. S-albumin was analysed according to DOUMAS et coll. (1971). Urinary excretions of calcium and phosphorus were determined on a non-restricted diet as the mean of three 24-hour excretions and expressed in mmol per mol excreted creatinine.

The bone mineral content (BMC) in the forearm was measured using a GAMMATEC osteodensitometer model GT 30 with a 185×10^7 Bq (50 mCi) ^{125}I source. The bone mineral concentration (BMC') was calculated as BMC/bone area

Table 2

Bone mineral content and bone mineral concentration in untreated hyperthyroid patients compared with normal controls. The values are given in arbitrary units and in per cent (in parentheses) of normal values

	Bone mineral content		Bone mineral concentration		Age (mean, range)
Patients					
Mean	38.5	(91.3)	15.7	(88.8)	46.4 (28–69)
SD	11.7	(16.6)	4.5	(19.6)	
SEM	2.6	(3.6)	1.0	(4.4)	
No.	20	20	20	20	20
Normal controls					
Mean	42.1	(101.1)	17.7	(100.2)	46.6 (29–68)
SD	7.7	(9.2)	3.1	(9.2)	
SEM	1.7	(2.1)	0.7	(2.1)	
No.	20	20	20	20	20
p	n.s.	<0.05	n.s.	<0.05	

(g/cm^3). The cross sectional bone area of the forearm was calculated from the equation:

$$\text{Bone area } (cm^2) = 1.35 \times (W_R + W_U) - 1.53,$$

where W_R and W_U are the width (cm) of radius and ulna, respectively, measured on the densitometric absorption curves. The equation was derived from densitometric and morphometric measurements of radius and ulna in the distal part of the forearm in 12 cadavers.

BMC and BMC′ were expressed in absolute values and in per cent of normal mean for the same age and sex. The reproducibility of BMC was about 1 per cent and of BMC′ about 3 per cent for normal individuals.

Statistical evaluations were performed using Spearman's rank correlation test and the Mann–Whitney test for comparisons of group means.

Results

Untreated hyperthyroidism. The chemical quantities measured fo calcium-phosphorus metabolism appear in Table 1. The serum concentration of calcium and the urinary excretions of calcium and phosphorus were significantly increased in the hyperthyroid patients compared with controls, whereas the serum concentrations of phosphorus were unchanged. The serum concentration of alkaline phosphatase was increased in untreated hyperthyroidism.

Table 2 gives BMC and BMC′ in hyperthyroid patients and in normal controls of

Table 3

Bone mineral content and bone mineral concentration in hyperthyroid patients following combined medical and surgical treatment. The values are given in arbitrary units and in per cent (in parentheses) of normal values

	Bone mineral content		Bone mineral concentration		Age (mean, range)	Bone mineral content		Bone mineral concentration		Age (mean, range)
Patients < 50 years of age						Patients ⩾ 50 years of age				
Mean	38.7	(89.0)	18.2	(99.8)	40.7 (28–49)	40.2	(100.8)	15.7	(97.4)	56.1 (51–68)
SD	8.7	(13.7)	4.0	(21.7)		7.6	(18.5)	2.0	(16.1)	
SEM	2.5	(4.0)	1.2	(6.5)		1.7	(4.0)	0.5	(3.8)	
No.	12	12	11	11	12	21	21	18	18	21
Normal controls										
Mean	42.9	(99.7)	18.2	(100.2)	40.5 (28–49)	41.3	(99.1)	16.3	(98.2)	56.0 (51–68)
SD	5.4	(9.9)	2.8	(13.5)		12.1	(15.1)	4.4	(18.9)	
SEM	1.6	(2.9)	0.8	(3.9)		2.6	(3.3)	1.0	(4.5)	
No.	12	12	12	12	12	21	21	21	21	21
p	<0.05	<0.05	n.s.	n.s.		n.s.	n.s.	n.s.	n.s.	

similar age and sex. In untreated hyperthyroidism a significant decrease was found in both BMC and BMC′. No relation could be demonstrated between BMC or BMC′ and the degree of hyperthyroidism expressed by the free thyroxine index ($S-T_4 \times S-T_3$-test) or by the absolute iodine uptake. Among the females a significant inverse correlation was found between BMC′ and age, both in hyperthyroid patients ($R=-0.63$, $n=18$, $p<0.01$) and in normal controls ($R=-0.62$, $n=18$, $p<0.02$), whereas no significant correlation was found between BMC and age. Therefore it was analysed whether the difference between the observed BMC′ in female hyperthyroid patients and the expected BMC′ according to the regression equation of BMC′ on age in normal controls, was correlated to thyroid function. However, no significant relationship could be demonstrated.

Treated hyperthyroidism. In treated hyperthyroidism BMC was subnormal in individuals below 50 years of age ($p<0.05$, $n=12$) and normal in individuals over 50 years of age (Table 3). For all individuals in the group no significant deviation was found in the mean BMC. BMC′ did not differ from normal in any of the age groups. No relation could be demonstrated between BMC or BMC′ and the time lag between the beginning of the antithyroid therapy and the investigation.

Discussion

A low bone mineral content (BMC) and low bone mineral concentration (BMC′) in relation to a control group was demonstrated in untreated hyperthyroidism. A morphometric evaluation of the amount of bone in the iliac crest in untreated hyper-

thyroidism showed a decrease in the amount of trabecular bone of 15 per cent and a decrease in the amount of cortical bone of 7 per cent due to an increased cortical porosity (MELSEN & MOSEKILDE 1977). In the present series a low BMC′ of the forearm of the same magnitude was demonstrated. The normal amount of osteoid relative to trabecular bone (MOSEKILDE et coll. 1977) and the normal phosphorus to hydroxyproline ratio (TOUGAARD 1976) in bone from hyperthyroid patients show furthermore that the observed changes in BMC and BMC′ in hyperthyroidism reflect variations in the total amount of bone and not in the degree of bone mineralisation.

The observed low amount of bone in untreated hyperthyroidism was followed by an increased urinary excretion of calcium and phosphorus and a slight increase in the serum calcium concentration. An increased dietary intake of calcium and phosphorus in the hyperthyroid state due to hyperphagia might contribute to these findings. However, both net and true intestinal calcium absorption has been reported to be decreased in hyperthyroidism (COOK et coll. 1959, SINGHELAKIS et coll. 1974) indicating that the main reason for the increased serum concentration and urinary excretion of calcium is an enhanced bone catabolism with an excess input of calcium into the plasma pool from bone. The increased serum level of alkaline phosphatase in hyperthyroidism reflects the enhanced bone formation in this state (MOSEKILDE et coll. 1977).

Similar values for BMC and BMC′ were found in treated hyperthyroidism as in normal controls except for slightly lower values in BMC in individuals less than 50 years of age. These findings support and elaborate previous biochemical, morphometric and densitometric results.

Roentgen ray densitometric measurements of metacarpal cortical bone and γ-ray measurements of the distal radius (FRASER et coll.) have demonstrated a decreased mean bone mineral content in untreated hyperthyroidism and a normal mean value in patients who had been euthyroid for more than a year after treatment with antithyroid drugs and surgery. On the other hand, patients treated with ^{131}I still had low values. These results indicate that the bone loss was reversible among younger patients treated with the combined therapy, and partly irreversible among older patients treated with ^{131}I. Furthermore, quantitative morphometric analysis of iliac crest biopsies (MOSEKILDE & MELSEN 1978) have demonstrated that the increased cortical porosity is completely normalized after 4 to 8 months of antithyroid therapy. The amount of trabecular bone, however, was unchanged and revealed a subnormal bone turnover and a decreased cellular activity.

Following antithyroid treatment the previous negative calcium balance is converted to a positive state (COOK et coll.). A rapid decrease in urinary excretions of calcium, phosphorus and hydroxyproline and an increase and subsequent decrease in serum alkaline phosphatase levels suggest similar changes in bone resorption and bone formation, respectively (SIERSBAEK-NIELSEN et coll. 1971, MOSEKILDE et coll. 1978).

The present findings indicate that a previous hyperthyroid state should not be considered a major risk factor for development of spontaneous fractures in the future providing the hyperthyroid state is effectively treated.

SUMMARY

Bone mineral content (BMC) and bone mineral concentration (BMC′) of the forearm were determined by photon absorptiometry in 20 untreated hyperthyroid patients and in 33 patients previously treated for hyperthyroidism. In untreated hyperthyroidism a significant decrease was found in both BMC and BMC′. In treated hyperthyroidism BMC and BMC′ were normalized. The findings suggest that a previous hyperthyroid state is not a risk factor for development of spontaneous fractures providing the hyperthyroid state is effectively treated.

ZUSAMMENFASSUNG

Der Gehalt an Knochenmineral (BMC) und die Knochenmineralkonzentration (BMC′) des Unterarms wurde durch Photonabsorptionsmessungen bei 20 unbehandelten hyperthyreoiden Patienten und bei 33 Patienten, die zuvor wegen eines Hyperthyreoidismus behandelt worden waren, festgestellt. Bei unbehandeltem Hyperthyreoidismus wird ein signifikanter Abfall von sowohl BMC und BMC′ gefunden. Bei behandelten Hyperthyreoidismus wurden BMC und BMC′ normal. Die Befunde lassen erkennen, dass ein vorheriger hyperthyreoider Status kein Risikofaktor für die Entwicklung von spontanen Frakturen ist, vorausgesetzt, dass der hyperthyreoide Status effektiv behandelt worden ist.

RÉSUMÉ

Le contenu minéral de l'os (BMC) et la concentration minérale de l'os (BMC′) de l'avant-bras ont été déterminés par une absorptiométrie de photons chez 20 malades hyperthyroïdiens non traités et chez 33 malades ayant subi un traitement por hyperthyroïdie. Dans l'hyperthyroïdie non traitée, les auteurs ont trouvé une diminution notable du BMC et de la BMC′. Dans l'hyperthyroïdie traitée le BMC et la BMC′ sont revenus à la normale. Ces résultats font penser qu'un antécédent d'état hyperthyroïdien n'est pas un facteur de risque pour l'apparition de fracture spontanée à condition que l'état hyperthyroïdien soit traité efficacement.

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