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POSTMENOPAUSAL BONE MINERAL LOSS AFTER TREATMENT FOR MALIGNANT GYNAECOLOGIC TUMOURS

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Loss of ovarian function is a side-effect or sometimes a desired result of the treatment of malignant gynaecologic tumours. After bilateral oophorectomy or radiologic castration, women of fertile age develop atrophy of different organs including the skeleton (AITKEN et coll. 1973, DALÉN et coll. 1974).

In an attempt to quantify the bone changes after treatment for malignant gynaecologic tumours, the bone mineral content was determined in a number of patients with normal menstruation before treatment. Special attention was paid to the effect of oestrogen deficiency on bone and both patients with and without oestrogen substitution were included in the series.

Material and Methods

Women still menstruating before treatment for malignant gynaecologic tumours were followed by annual bone mineral measurements over a period of 4 years. Patients with recurrence of the tumour during the observation period were excluded and the series thus consisted of 9 patients treated for cervical carcinomas and 3 for endometrial carcinomas. All patients had been given preoperative brachy-radium irradiation followed by simple hysterectomy or radical hysterectomy according to Wertheim-Meigs and bilateral salpingo-oophorectomy. The first bone mineral measurement was made within 3 to 6 months after the operation.

Five of the patients with cervical carcinoma received oestrogen substitution (Promarit 0.625 mg or Progynon 1 mg daily for 3 weeks followed by one week without medication). The indication for oestrogen substitution was prevention of postmenopausal symptoms. The selection of patients for this therapy was partly dependent on the clinician's personal evaluation of the hazards of such a therapy.

Furthermore, the bone mineral content was determined once in 29 women who had been treated for ovarian carcinoma 5 to 15 years previously. These patients had undergone bilateral oophorectomy and complementary external irradiation and had not been given oestrogen substitution.

The bone mineral content was assayed by roentgen spectrophotometry (JACOBSON 1964). This method is based on attenuation measurements at two radiation energies from a roentgen tube. The bone to be examined is positioned by TV-fluoroscopy and the mineral content of the bone is determinded by scanning with a radiation beam. The left forearm (1 and 8 cm from the radiocarpal joint, respectively) and the right femur (neck and midshaft) were chosen for measurement of the mineral content (cf. DALÉN & JACOBSON 1974). The change in mineral content at each site was calculated by linear regression of 4 measurements made yearly. For each individual, the mean change of the 4 sites was calculated. The statistical evaluations were made according to Student's t-test.

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Table 1

Annual change in bone mineral content in oophorectomized women

	Substituted (n=5)		Non-substituted (n=7)		Difference		
	Mean (per cent)	SD	Mean (per cent)	SD	Per cent	t	p
Radius + ulna, distal	+5.2	4.0	−3.0	2.5	−8.2	4.37	<0.05
Radius + ulna, shaft	+0.4	5.1	−2.3	2.5	−2.7	1.19	>0.05
Femur, neck	−0.6	3.2	−4.7	3.4	−4.1	2.12	>0.05
Femur, shaft	−1.0	7.7	−3.0	3.4	−2.0	0.62	>0.05
Mean of 4 sites	+1.0	3.9	−3.3	1.8	−4.3	2.57	<0.05

Table 2

Bone mineral content in oophorectomized women. The mineral content is expressed in per cent of the content in group I

Time after oophorectomy	Group I Within 3 months (n=12)		Group II 5–10 years (n=13)		Group III 10–15 years (n=16)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	42	6	45	7	44	6
Bone mineral, mean of all sites (per cent)	100	11	91	8	89	11
Bone mineral, mean of trabecular sites (per cent)	100	11	86	9	85	15

Results

The non-substituted women lost about 3 per cent of their initial bone mineral content per year, whereas the bone mineral content increased by one per cent a year in the substituted group (Table 1). The difference in the change in bone mineral content was significant ($p<0.05$), and was greater at sites containing trabecular bone (the distal forearm and the femoral neck) than in parts containing mainly cortical bone (midshaft of the forearm and the femur). Women who had undergone bilateral oophorectomy 5 to 10 years previously had considerably lower bone mineral content than those recently operated upon (Table 2).

Discussion

It can be speculated as to whether several factors are involved in the bone changes in patients with malignant gynaecologic tumours. Oestrogen deficiency is one factor, but it is also possible that the inactivity after the surgical trauma or malabsorption due to irradiation of the guts contributes to the bone mineral loss. However, it is reasonable to assume that oestrogen deficiency is the most important factor as the group with oestrogen substitution did not lose bone mineral.

The effect of oestrogen deficiency on the bone tissue has been under discussion since 1941 when ALBRIGHT et coll. suggested an association between menopause and osteoporosis. With the introduction of the mineral measurement methods, it was possible to demonstrate that postmenopausal women lose bone mineral and that oestrogen substitution prevents, or at least retards, the bone mineral loss in both artificial and natural menopause (AITKEN et coll. 1973, LINDSAY et coll. 1980).

The method used in this series permits measure-

ments of the bone mineral content in nearly all parts of the skeleton. Previously, it was demonstrated that oophorectomized women have a reduced bone mineral content in both central and peripheral parts of the skeleton and that the reduction is particularly great in parts of the skeleton rich on trabecular bone, e.g. the distal forearm, the spine and the femoral neck (DALÉN et coll. 1974). Thus, the reduction of bone mineral is particularly great at sites where postmenopausal women have a high incidence of fractures.

The present data indicate that bilateral oophorectomy is followed by a general loss of bone mineral, although more marked in trabecular than in cortical bone. The loss of bone mineral is great in the years immediately after oophorectomy and appears to diminish with time (cf. AITKEN et coll.).

The practical implication of the present findings is that non-substituted patients probably develop postmenopausal osteoporosis with an increased risk of fractures. This risk, the magnitude of which can only be estimated by fracture epidemiologic investigations, should be considered in the discussion on the advantages and disadvantages of oestrogen substitution in these patients.

SUMMARY

Bone mineral content after treatment for malignant gynaecologic tumours was examined in women of fertile age. The treatment given was intracavitary radium applications followed by bilateral oophorectomy. In women who received oestrogen substitution the bone mineral content increased by one per cent a year, whereas non-substituted women lost 3 per cent of their initial bone mineral content per year. The findings suggest that oestrogen deficiency is the predominant cause of bone mineral loss initiated by this therapy.

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