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Bone Mineral Content of the Third Lumbar Vertebra during 18 Months of Prednisolone Treatment for Giant Cell Arteritis

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Summary **Altogether forty-four patients with giant cell arteritis (GCA) were randomly allocated to either daily morning or alternate-day administration of prednisolone. The BMC of the third lumbar vertebra was determined using dual photon absorptiometry. At least ten measurements were performed in each patient during a period of 18 months. During the course of treatment there was no significant change of the mean BMC in either group compared to the pre-treatment value. The changes of BMC were independent of such potentially explanatory variables as cumulative dose of prednisolone, initial BMC, sex and body weight. Corticosteroid treatment in patients with GCA, in the doses used by us, does not appear to cause excessive bone loss.**

Key words **Osteoporosis, Dual Photon Absorptiometry, Polymyalgia Rheumatica, Temporal Arteritis, GCA, Corticosteroids.**

INTRODUCTION

Giant cell arteritis is an important disease in elderly people which can be treated effectively with corticosteroids thus preventing ischaemic catastrophies and giving relief to the patient (1,2). Osteoporosis is a major complication of steroid treatment and thought to be a threat to patients on long-term treatment even if the doses of corticosteroids are moderate (3,4).

We here report the results of repeated measurements of the bone mineral content (BMC) of the third lumbar vertebra in 44 patients during a period of 18 months. Two different treatment regimens are compared.

PATIENTS AND METHODS

Patients

Thirty-six women and 8 men aged between 50 and 87 years (mean age 71.3 years) were consecutively recruited to the present study. One woman was 50 years of age and terminated menopause 2 years earlier. All the other women were beyond 60 years and postmenopausal since many years. In 16 of the patients, a biopsy of the temporal artery demonstrated arteritis characterized by the histological findings of the interruption of the internal elastic membrane and the infiltration of mononuclear cells into the arterial wall. Giant cells were often found, but their presence was not required for diagnosis. In the remaining biopsy-negative subjects, the diagnosis of GCA was founded on either symptoms and signs of temporal arteritis (TA) or the clinical criteria for polymyalgia rheumatica (PMR) as used by Bengtsson and Malmvall (5).

Controls

A control population consisting of 214 normal women aged between 35 and 80 years from Göteborg, a city on the west coast of Sweden, was selected at random from the Revenue Office Register in Göteborg (6). The BMC was determined using dual-photon absorptiometry in L3.

Study protocol

None of the patients had been treated previously with corticosteroids and none had suffered from diseases known to affect bone metabolism. No patients had sup-

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Table I: *The patients were allocated randomly to either daily (Group I) or alternate-day (Group II) administration of prednisolone. The table shows the daily doses each week according to the planned treatment regimens*

Every day (Group I)		Alternate day (Group II)	
Week	Dose	Week	Dose
1	40	1	40
2	25	2	25
3	20	3	20
4	15	4	15
5-6	15	5-6	17.5/12.5
7-8	15	7-8	20/10
9-10	12.5	9-10	22.5/7.5
11-12	12.5	1-12	25/5
13	12.5	13	27.5/2.5
14	10	14	27.5/2.5
15-16	10	15-16	30/0
17-18	10	17-18	27.5/0
19-20	7.5	19-20	25/0
21-22	7.5	21-22	22.5/0
23	7.5	23	20/0
24	5	24	20/0
25-26	5	25-26	17.5/0
27-28	5	27-28	15/0
29-30	5	29-30	12.5/0
31-32	5	31-32	10/0
Maintenance dose	2.5-5	Maintenance dose	5-10/0

plements with calcium or hormone replacement therapy. Some of the patients were on diuretic therapy for a mild or moderate hypertension but no alteration in the dose was made during the study. The patients were allocated randomly to either a daily morning administration of prednisolone (Group I: 6 men, 18 women; mean age 70.1 years) or a daily morning dose of prednisolone followed by a gradual transfer to alternate-day treatment (Group II: 2 men, 18 women; mean age 72.3 years). The starting dose averaged 36 mg of prednisolone (all patients) and was followed by gradual decrements according to clinical and laboratory responses (Table I). Details of treatment are given in Table II.

Bone mineral content (BMC)

The BMC was determined in the third lumbar vertebra (L3) using dual photon absorptiometry and expressed in g/cm2 (BMA) as well as in g/cm (BMC). The latter unit was chosen, since we have found that the strength properties of the lumbar vertebrae are better represented by the use of g/cm (7,8). Dual-photon absorptiometry involves the use of two radionuclides, 241 Am and 137 Cs, both of which emit gamma radiation at different energy levels. The gamma radiation passes the object to be measured in a narrow collimated radiation beam. The transmitted radiation of both energy levels is simultaneously registered by a scintillation detector which is connected, via pulse height electronics, to a computer. An electronic control unit permits intermittent scanning in steps of 4 mm. Transmission measurements are made between the steps at preselected time intervals. The bone mineral content at each measuring point, 33 in all, is estimated assuming exponential attenuation of the two photon energy levels. The plotting of each point versus the position over the vertebra produces what is known as a bone profile curve. Points outside the bone on both sides are selected to form the endpoints of a baseline above which the bone profile curve is integrated, thereby yielding the bone mineral content in units of g/cm previously described in a more detailed manner (9,10).

The BMC was determined immediately before the administration of corticosteroids and monthly measurements were then made during the first four months of treatment. Later, the BMC was determined every 3-4 months. At least ten measurements were made during a follow-up period of 18 months.

Statistical methods

The linear regression functions of the BMC and BMA as a function of age were determined for patients and controls. Comparisons of the parameters of the regression functions were made using t-tests. The change in the BMC and BMA respectively during treatment was tested using Fisher's test for pair comparisons (11). A second order regression model was used in order to estimate the change in the BMC and the BMA as a function of time since the start of treatment. Pitman's test (11) was used to test the correlation between the BMC% and BMA%, respectively and some variables, such as age, sex, body weight, body mass index, initial BMC and cumulative dose of prednisolone. Two-sided tests were used.

RESULTS

Prior to treatment, the BMC as well as BMA were similar in the patients and in the control subjects. This is borne out by Fig. 1 (A and B), which shows the BMC in both groups in relation to age (Fig. 1). The BMC averaged 3.88 g/cm (range 2.18-5.39) in Group I and 3.81 g/cm (range 2.73-6.01) in Group II.

Although the individual variation was considerable, neither the average BMC nor the BMA differed signif-

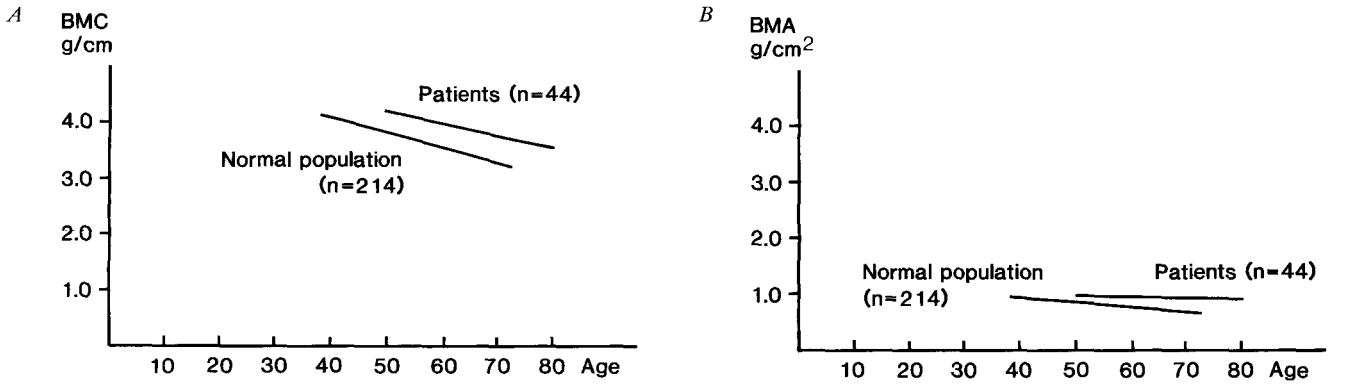

Fig. 1: Bone mineral content (expressed in units of g/cm and g/cm2) in patients compared with normal controls of different ages. The regression functions were similar in patients and controls.

icantly from the pre-treatment value at any single measurement point. The mean BMC and BMA expressed as a percentage of the pre-treatment value (BMC%, BMA%) was estimated at certain intervals (see Methods) from a second order regression function (Fig. 2 A,B). These values which estimated the BMC% and BMA% at the same time after the start of therapy in all subjects never differed by more than 5% from the original value (95 per cent confidence interval). As Figure 2 shows, there was an insignificant decrease in the estimated BMC% and BMA% (with a decrease of 2.6% and 3.4%, respectively) during the first year. After 18 months, however, the decrease was only 1.5% for BMC and 1.9% for BMA compared with the pre-treatment value.

At the end of the study there was no difference in the percentage changes in the BMC in relation to the original value between the patients in Group I and Group II. A statistical analysis also revealed that changes in the BMC and BMA were independent of certain explanatory variables such as age, sex, body weight, body mass index, initial BMC and cumulative dose of prednisolone.

In three female subjects, crush fractures of the vertebrae occurred after 4, 12 and 18 months of treatment. Their initial BMC values were 3.27, 3.54 and 2.18 g/cm respectively. In none of them had the BMC decreased more than 5% at the last measurement prior to the crush fracture. The third lumbar vertebra was

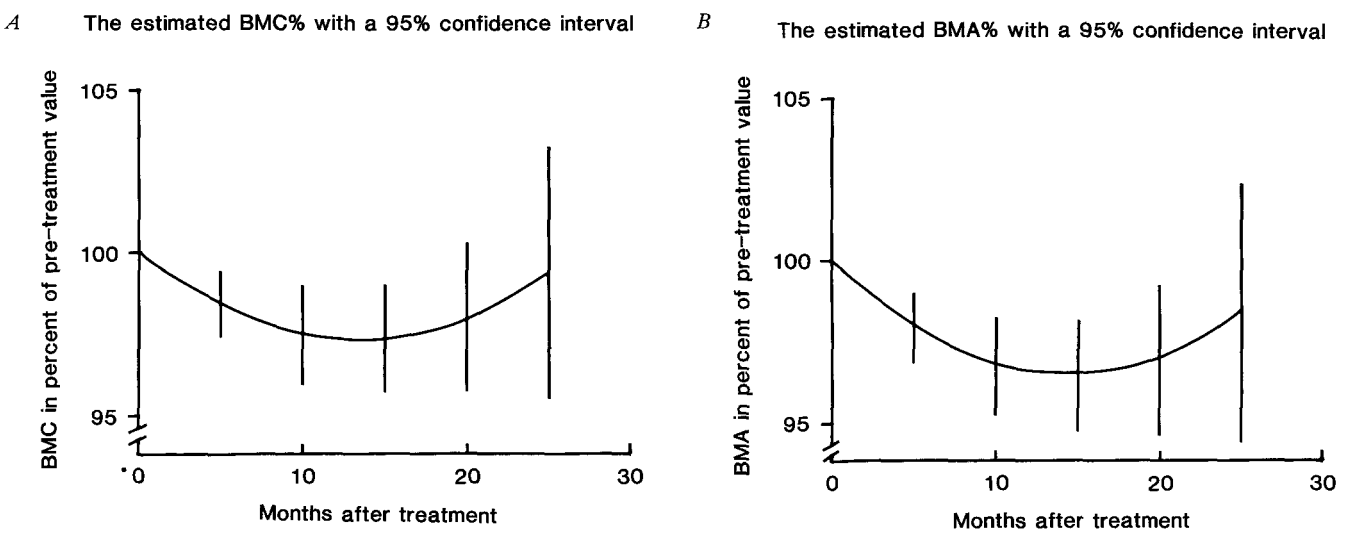

Fig. 2: The mean BMC expressed as a percentage of the pre-treatment value, BMC%, was estimated from a second order regression function (see Methods), thus permitting the assessment of BMC% at specific intervals. The mean BMA was treated in the same way. These BMC% and BMA% never differed by more than 5% from the first BMC% and BMA% value (95% confidence interval).

Table II: *Administered cumulative dose of prednisolone (mg) of the two treatment groups. The calculated dose according to the planned treatment regimens is given within brackets*

Group I (Every day treatment)		Group II (Alternate day treatment)		Months
0	(0)	0	(0)	0
690	(700)	736	(700)	1
1112	(1120)	1151	(1120)	2
1483	(1470)	1566	(1540)	3
1801	(1767)	1986	(1960)	4
2513	(2345)	2903	(2812)	7
3481	(3185)	3920	(3492)	13
4127	(3885)	4572	(4017)	18

not involved in any of them and they all remained in the study.

Compared with the dose of corticosteroid in the treatment regimen, both groups had been given a slightly higher cumulative dose of prednisolone in order to control the disease (Table II). Two patients were unable to manage alternate-day therapy and were transferred to daily administration after 3 and 5 months respectively.

DISCUSSION

In this prospective study we were unable to demonstrate any significant decrease in bone mineral content of vertebra L3 in giant cell arteritis patients who had been treated with corticosteroids, regardless of whether the steroids were administered in a daily morning dose or on alternate days.

The bone mineral content was assessed using dual-photon absorptiometry. This method has a short term in vivo precision of 3%, and a long term reproducibility of less than 2% (9,10). Thus, an average difference in bone mineral content of 1% in the entire group would be detected. An annual decrease in the BMC of about 0.5-1.% would be expected in this age group (6). In both sexes a similar rate of bone loss would be anticipated in healthy subjects.

If body weight were to increase during corticosteroid treatment, it is possible that our technique would overestimate the BMC. There was, however, no relationship between changes in the BMC and body weight in our study.

Osteoporosis has been recognized as a serious sequela of hypercortisolism (3,13). Steroid-induced osteoporosis is more marked in trabecular than in cortical bone (14). As most studies of osteoporotic complications have been retrospective (14-21), it has been difficult to relate the severity of bone loss to the duration and dose of steroids. In some other studies, neither the dose (17,18) nor the duration of treatment was specified (15,18,23) or else high doses (> 15mg prednisolone per day) were used (14-16, 22, 24, 25).

Long-term prospective well-controlled studies on glucocorticoid-induced bone loss in the axial skeleton are limited. Most studies have measured bone density in the distal radius (16,21,22,24,26), but bone loss in the distal radius correlates less well with changes in the spine (27).

Ruegsegger (24) measured trabecular bone of the distal tibia and the radius prospectively using quantitative computed tomography in patients with bronchial asthma on alternate-day corticosteroid treatment and found a dose-dependent decrease in bone volume after one year of treatment. Interestingly, no decrease in bone volume was found in a subgroup of patients who were given a low maintenance dose (< 17 mg of prednisolone every other day). Controversy still exists as to whether there is a safe dose level for corticosteroids with respect to bone. Premenopausal women with rheumatoid arthritis, who were treated with low doses of steroids, did not lose bone mineral in a well-conducted longitudinal study by de Deuxchaisnes (26). Sambrook (19) obtained similar results and concluded that low doses of corticosteroids are safe in patients with rheumatoid arthritis. Als (21), on the other hand, reported a significant reduction in bone mineral content of the distal radius in premenopausal women, but not in postmenopausal women.

In the treatment of GCA higher doses of corticosteroids are given only during the initial phase of the disease or at times of flare-up. After a few months most patients can be controlled by a low maintenance dose of 5-7.5 mg of prednisolone, and this might explain why the bone mineral content did not change in this study.

Only a few studies of bone mineral content have previously been performed in patients suffering from GCA. In a retrospective study of patients treated with corticosteroids for an average period of five years, Andersson et al. (28) were unable to demonstrate any difference in the bone mineral content of the heel bone compared with normal controls of the same age. In another study (23), the total body calcium was not affected in 12 patients with polymyalgia rheumatica treated with corticosteroids. On the other hand, the total body calcium of patients with rheumatoid arthritis on the same low doses of corticosteroids decreased.

The disorders for which corticosteroids are prescribed could themselves have significant effects on the skeleton. In the case of inflammatory diseases there are important relationships between the immune system and

both the local and the systemic regulation of bone metabolism (29).

The way in which the steroids are administered could also have an important effect on the development of osteoporosis. We gave prednisolone in a single morning dose. Sometimes other schedules comprising two or three doses a day are recommended. Administering corticosteroids in this way is known to suppress the pituitary-adrenal axis more than a single morning dose does. It is, however, uncertain whether such a regimen is less perilous for the bone.

We observed a tendency towards an insignificant initial decline in bone mineral content followed by a subsequent increase. This may not necessarily reflect changes in the doses of corticosteroids during the course of therapy or the fact that corticosteroids induce more bone loss at an early stage as has been suggested (22). In addition to the possibility that the disease itself might influence bone mineral content, the patients are also hampered in their physical activity. After treatment has started, the symptoms of the disease quickly disappear and the patients regain their physical fitness. The importance of physical activity to bone mass is well documented (30).

According to our study corticosteroid treatment of patients suffering from GCA, in the doses used by us, appears not to cause excessive loss of bone mineral content (6) of the third lumbar vertebra. Extended studies comprising other parts of the spine would be of interest, and such studies are under progress in our department.

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