Loss of bone mineral density in premenopausal women with systemic lupus erythematosus

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Abstract

Objective—To evaluate bone mineral density (BMD) in premenopausal patients with systemic lupus erythematosus (SLE).

Methods—We measured BMD by dual energy x-ray absorptiometry at lumbar vertebrae L2-4 and at the right femoral neck in 74 premenopausal white patients (mean age 30.8 years) with SLE who were receiving glucocorticoid therapy, and in a control group.

Results—The mean cumulative dose of prednisone was 32.5 (SD 28) g. The mean dose at the time of absorptiometry was 13.7 (6.9) mg. BMD was significantly reduced at the spine and at the femoral neck in SLE patients when compared with the control group: L2-4 = 0.943 (0.1) g/cm2 v 1.038 (0.1) g/cm2 (p < 0.001); femoral neck = 0.766 (0.09) g/cm2 v 0.864 (0.1) g/cm2 (p < 0.001). Nine patients (12.1%), but none of the control group, had a BMD less than the reference range.

Conclusion—BMD in premenopausal patients with SLE was less than that in a control group and less than the reference range of values defining the presence of osteoporosis in 12.1%. We did not find a relationship between BMD and either cumulative or baseline dose of corticosteroid therapy.

(Systemic lupus erythematosus (SLE) is an inflammatory disease resulting in multisystem damage. The clinical course is characterised by periods of remission and relapses. It mainly affects women in their reproductive years, and they often have irregular menstrual cycles. Most of the patients need glucocorticoid therapy to control the disease activity.

These factors suggest that osteoporosis is likely to be a complication in SLE. Surprisingly, there are few reports on bone mineral density (BMD) in SLE. The aim of the present study was to analyse BMD in a population of premenopausal SLE patients receiving glucocorticoid therapy.

Patients and methods

We followed closely the clinical course of 150 white patients who fulfilled at least four American Rheumatologists Association criteria for SLE. We evaluated all the premenopausal patients and included in the study 74 patients who fulfilled the following criteria: age greater than 16 years; one year or more of evolution of the disease; glucocorticoid therapy received at some stage of the disease; serum creatinine concentrations <1.3 mg/dl; no coexisting condition (intestinal malabsorption, liver disease, hyperparathyroidism) that could interfere with bone metabolism; no previous or current therapy with drugs known to affect bone metabolism (including anticonvulsants, barbiturates, oestrogenic hormones, androgenic hormones, sodium fluoride, calcitonin, supplementary calcium, thiazide or anticoagulant drug therapy); functional class I or II according to Steinbrocker et al; no significant history of alcohol consumption; no history of smoking, or fewer than 100 cigarettes in their lifetime.

The following data were recorded: age; age at onset of disease; duration of disease (months); cumulative dose of corticosteroids (prednisone or equivalent); dose of corticosteroids at the time that densitometry was performed (prednisone or equivalent); mean dose of corticosteroids/year; disease activity of the lupus patients, assessed with the University College Hospital/Middlesex SLE scoring system with a numerical score of disease activity graded from 1 to 4 (inactive to severely active disease); presence of 12 or more months of amenorrhoea (the periods of amenorrhoea not necessarily concurrent; information was sought concerning lack of bleeding during periods of at least 3 months duration); calcium intake (dietician’s estimate based on review of food consumption during the eight weeks before testing).

The control group comprised 50 premenopausal women who were volunteers taking part in a screening programme of age related bone loss. They had similar age, weight, and height distribution, and regular menstrual cycles. Those with diseases or treatments that could interfere with bone metabolism were excluded.

Using ultrasensitive film in order to minimise the exposure to x-rays, we obtained anteroposterior and lateral radiographs of the thoracic and lumbar spine, and anteroposterior radiographs of the hip in all the SLE patients and the control group.

In both groups of subjects, BMD in the lumbar spine and femoral neck was measured by dual energy x-ray absorptiometry (DXA) using a densitometer (Hologic QDR 1000). The regions of interest analysed in the lumbar spine were L2, L3, and L4 (giving a mean value for L2-4); in the right hip, the femoral neck was chosen. Calibration of the technique against a lumbar spine phantom was performed daily and with a femoral phantom...
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Bone loss is a normal part of aging; measurement of bone mineral content was accurate to within 0.5% compared with the Hologic X-caliber QDR-1 Anthropomorphic Spine Phantom of known mineral content, and precision of measurement was better than 0.01 g/cm² (coefficient of variation 1-0% at BMD 1·0 g/cm²). Patients received doses of radiation in the range 2–5 mrem (0·02–0·05 Sy) per scan.

According to established criteria, we defined osteoporosis as present when the BMD of the lumbar spine was 2 SD less than the mean of that age group which includes subjects 20–40 years old, utilising the results of a multicentre Spanish study of 2442 patients (1305 women), analysed by DXA. The relevant reference value for L2–4 was <0·793 g/cm².

Vertebral fracture was defined as a reduction of at least 20% in anterior height compared with posterior height.

Results were expressed as mean (SD) and were analysed by Z test. Multiple linear regression was used for analysis of BMD of lumbar spine and femoral neck with cumulative dose and dose at the time of DXA. Results were considered significant when p < 0·05.

Results

The mean age of the 74 SLE premenopausal patients was 30·8 (6·5) years (range 17–44 years), mean age at disease onset was 23·6 (7·6) years (range 11–43 years), and mean duration of disease was 86·4 (60·7) months. In the control group the mean age was 30·8 (6·9) years (range 16–44 years).

The mean cumulative dose of prednisone was 32·5 (28·5) g (range 2·7–116·4 g), with an average of 4·5 g/year (mean daily dose 12·32 mg). The mean dose at the time of absorptiometry was 13·7 (6·9) mg/day (range 0–50 mg/day). Fifty four patients (72·9%) were receiving alternate day therapy.

Three patients (4%) had 12 or more months of amenorrhoea.

Mean dietary calcium intake in all the SLE patients was 955 (400) mg per day. At the time of DXA the mean disease activity grade was 2·43 (0·7).

No patient or control had vertebral fractures.

BMD was significantly decreased at the spine and the femoral neck in SLE patients compared with the control group (table 1); L2–4 0·943 (0·1) g/cm² v 1·038 (0·1) g/cm² (p < 0·001); femoral neck 0·766 (0·09) g/cm² v 0·864 (0·1) g/cm² (p < 0·001).

Among the SLE patients, nine (12·1%) had BMD below the reference range for young females which defined osteoporosis; one of these nine had amenorrhoea. In the control group none had BMD values below the reference range. There were no statistical differences between the variables studied in the nine SLE patients with osteoporosis compared with the 65 SLE patients without osteoporosis.

There was no correlation between the dose of prednisone at the time of densitometry or the cumulative dose and BMD at the lumbar spine or femoral neck, and no difference in BMD between patients receiving daily or alternate day steroid therapy.

We did not find correlation between disease duration or mean disease activity grade and BMD.

Discussion

Most studies of osteoporosis in patients with autoimmune disease have been in those with rheumatoid arthritis.1–10 There has been little investigation of osteoporosis in patients with SLE.1–11

Our study using dual energy x ray absorptiometry has shown a high percentage of patients with low BMD in a population of 74 SLE young, premenopausal subjects: nine of our patients (12·1%) had BMD below the reference range indicating osteoporosis. We found the bone mass of the lumbar spine and femoral neck to be less in this group of SLE patients than in control subjects (p < 0·001). Fractures were not found. Our patients had a high mean cumulative dose of prednisone and a high mean dose of prednisone at the time of the study, but we did not find any relation between dose of glucocorticoid therapy and BMD in the lumbar spine or femoral neck. In addition, we did not find any correlation between BMD and disease duration or the disease activity.

Our results confirm those of Dhillon et al16 and Kalla et al17 in premenopausal SLE patients, which also showed no correlation between cumulative dose of prednisone and BMD, and no fractures. However, Dhillon et al19 found a lower frequency of osteoporosis, reporting a low BMD in one (4·5%) of 22 SLE patients—admittedly a small sample size. In the more recent report of Kalla et al,20 25% of 46 SLE patients had BMD below the reference range.

Glucocorticoid therapy,12 amenorrhoea,13 hyperparathyroidism secondary to chronic renal failure,14 amenorrhoea,15–17 and reduced gonadal steroid secretion.25 Bone loss is most rapid in areas of the skeleton containing the greatest proportion of trabecular bone.24 While the exact incidence of osteoporosis in patients receiving glucocorticoid therapy remains unknown, figures of 30–50% have been reported.25 26 The dose of prednisone that inhibits bone formation has not been identified.

Amenorrhoeic young women participating in intensive exercise, and those with anorexia nervosa,13 hypogonadotrophic hypogonadism,22 hyperprolactinaemia,28 or premature menopause29 also have reduced bone mass. Some studies30 31 have suggested that factors
produced in the inflammatory mechanism of SLE may be implicated in disturbances of bone mineral metabolism which lead to osteoporosis. Tanaka et al.31 observed spontaneous production of bone resorbing lymphokines in SLE patients in the absence of corticosteroid therapy. In view of their own results and the observation of Lahita et al.32 of increased rates of 16-α hydroxylation of oestradiol in lupus patients with the formation of oestrogenic production of bone resorbing lymphokines in that lupus patients may be oestriol, Dhillon et al.of observation of Lahita et al.32 of lupus patients with hypogonadism. Abnormal corticosteroid-induced osteopenia in patients with rheumatic diseases. Arthritis Rheum 1985; 28: 361-8.


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