Brazilian Journal of Medical and Biological Research (2002) 35: 1159-1163
ISSN 0100-879X

Bone mineral density in juvenile systemic lupus erythematosus

T.C.M. Castro[1], M.T. Terreri[1], V.L. Szejnfeld[2], C.H.M. Castro[2], M. Fisberg[1], M. Gabay[1] and M.O.E. Hilário[1]

[1]Divisão de Alergia, Imunologia e Reumatologia, Departamento de Pediatria, and [2]Divisão de Reumatologia, Departamento de Medicina, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brasil

Correspondence
M.T. Terreri
Rua Loefgreen, 2381, apto 141
04040-004 São Paulo, SP
Brasil
Fax: +55-11-5579-1590
E-mail: terreri@uninet.com.br

Research supported by CNPq.
Publication supported by FAPESP.

Received October 30, 2001
Accepted August 6, 2002

Abstract

We evaluated spine bone mineral density (BMD) in Brazilian children with juvenile systemic lupus erythematosus (JSLE) in order to detect potential predictors of reduction in bone mass. A cross-sectional study of BMD at the lumbar spine level (L2-L4) was conducted on 16 female JSLE patients aged 6-17 years. Thirty-two age-matched healthy girls were used as control. BMD at the lumbar spine was measured by dual-energy X-ray absorptiometry. Weight, height and pubertal Tanner stage were determined in patients and controls. Disease duration, mean daily steroid doses, mean cumulative steroid doses and JSLE activity measured by the systemic lupus erythematosus disease activity index (SLEDAI) were determined for all JSLE patients based on their medical charts. All parameters were used as potential determinant factors for bone loss. Lumbar BMD tended to be lower in the JSLE patients, however, this difference was not statistically significant ($P = 0.10$). No significant correlation was observed in JSLE girls between BMD and age, height, Tanner stage, disease duration, corticosteroid use or disease activity. We found a weak correlation between BMD and weight ($r = 0.672$). In the JSLE group we found no significant parameters to correlate with reduced bone mass. Disease activity and mean cumulative steroid doses were not related to BMD values. We did not observe reduced bone mass in female JSLE.

Key words
- Systemic lupus erythematosus
- Children
- Adolescents
- Bone mineral density
- Osteoporosis
- Corticosteroids

Introduction

Osteoporosis is a major public health problem affecting postmenopausal women and older persons in general. Due to improvements in instrumentation we can now detect this condition in children.

Significant osteopenia has been detected in children with diseases such as juvenile dermatomyositis, juvenile rheumatoid arthritis and juvenile systemic lupus erythematosus (JSLE) (1-5). Multiple causes have been proposed to contribute to osteopenia, including limited physical activity, immobility, limited exposure to sunlight, systemic inflammation, corticosteroid use, delay in pubertal development, inadequate dietary intake of calcium and vitamins, and renal insufficiency (3,5-10). Although there is no consensus about the extent of the impact of these factors on bone mineral density (BMD) in children with rheumatic diseases, it is important to understand their implications in order to plan further strategies to prevent and treat bone disease in these children. The objective of the present study was to assess BMD in

normal and JSLE Brazilian children in order to determine potential predictors of bone mass modifications.

Material and Methods

Patients

We studied 16 girls aged 6 to 17 years with JSLE diagnosed according to the American College of Rheumatology criteria for the classification of systemic lupus erythematosus (SLE) (11). As a control group we evaluated 32 age-matched healthy girls from the community. The study protocol was approved by the Ethics Committee of Universidade Federal de São Paulo and written informed consent was obtained from all parents or guardians.

Weight and height were measured in patients and controls using an anthropometric balance. Tanner stage was assigned by a pediatrician as determined by physical examination. Patients were classified into two groups: i) group 1, consisting of girls within the G1-G2 Tanner range, and ii) group 2, consisting of G3-G5 girls. This division was based on the fact that patients with Tanner G3 or higher usually present increased bone mass (12). Duration of disease was considered as the period of time from the first clinical manifestations to the evaluation by densitometry. Mean daily steroid doses and mean cumulative steroid doses of prednisone were calculated from medical charts for every patient.

For the children with JSLE, medical charts were reviewed and current disease activity was assessed by the SLE disease activity index (SLEDAI). We considered active disease to be present when SLEDAI was >10.

Dual-energy X-ray absorptiometry

BMD at the lumbar spine level (L2-L4) was measured in all subjects by dual-energy X-ray absorptiometry using a LUNAR DPX densitometer (Lunar Radiation Corporation, Madison, WI, USA). In our Densitometer Unit this instrument has a coefficient of variation of 2.0% at the lumbar spine in children.

Statistical analysis

The Student *t*-test was used to compare BMD of patients and controls. The χ^2-test was used to compare BMD of controls and JSLE patients with Tanner stage. In the JSLE group, Pearson's correlation coefficient was used to detect potential associations between BMD and anthropometric measures, disease duration, mean daily steroid doses and mean cumulative steroid doses. The Student *t*-test was also used to compare BMD of patients with Tanner stage and disease activity. All statistical analyses were performed using the SPSS software version 8.0. A P value of <0.05 was considered to be statistically significant.

Results

Sixteen female patients with JSLE and 32 aged-matched healthy girls were included in this study. Data considering age, weight, height, disease duration, cumulative and daily doses of prednisone and BMD values for both groups are shown in Table 1. Mean duration of disease was 3.9 ± 2.7 years.

Most patients had been taking corticosteroids during the course of their disease. All patients with JSLE were treated with corticosteroids and at the time of evaluation all but one were taking this medication. The mean daily steroid dose was 0.54 ± 0.42 mg kg^{-1} day^{-1} and the mean cumulative steroid dose was 14.2 ± 11.3 g. In the JSLE group, 4 patients were in stage G1-G2 and 12 were in stage G3-G5. In the control group, 10 individuals were in stage G1-G2 and 22 were in stage G3-G5. Pubertal development did not differ significantly between the two groups. Mean SLEDAI score for the JSLE group

was 7.7 (range: 0-28). According to the SLEDAI, 11 children presented inactive disease (SLEDAI between 1 and 10) and 5 had active disease (SLEDAI higher than 10).

Except for height, the two groups were similar (age, weight, and Tanner stage) and did not show any statistically significant difference. As can be seen in Table 1, BMD values in the JSLE group were not statistically different compared with those seen in the control group (P = 0.10).

In the JSLE group, we did not observe a significant correlation between BMD and age, height, disease duration or corticosteroid use. A statistically significant correlation was observed between BMD and weight (r = 0.672). There were no significant BMD differences between JSLE stages G1-G2 and stages G3-G5 (0.839 *vs* 0.848 g/cm^2) or between patients with and without disease activity.

Discussion

Although some information concerning BMD in adults with SLE is available (13-15), few data on children and adolescents have been reported (1,16,17). Steroids are a mainstay of drug therapy in SLE and are a well-recognized cause of osteoporosis in rheumatoid arthritis and other conditions such as asthma (18-21). Adult patients with SLE present low bone mass at peripheral and axial skeletal sites mainly related to steroid treatment (22).

Our results did not demonstrate that children with JSLE present a reduced bone mass at the lumbar spine level compared to healthy children. JSLE patients usually do not present significant muscle or joint involvement, which, in our opinion, would be the most important determinant factor for a reduction of bone mass in diseases like juvenile rheumatoid arthritis and juvenile dermatomyositis. Differently from adult patients with SLE, our study showed that in children with JSLE there is no significant correlation between bone mass and steroid use. The Student *t*-test did not demonstrate a clear impact of corticosteroid use on lupus children's BMD. An influence of corticotherapy was not observed probably due to the period between the beginning of the treatment and the posterior study enrollment. In other words, many patients were not already taking high doses of corticosteroids at the beginning of the study. Some other studies have demonstrated a role of steroids in determining bone loss in JSLE children. However, Falcini et al. (17) observed a reduction in both lumbar spine BMD and calcaneal ultrasound measurements in 53 patients affected by juvenile rheumatoid arthritis (N = 29), JSLE (N = 13) and juvenile dermatomyositis (N = 11) compared with a control group. All patients with JSLE were taking corticosteroids. Using a longitudinal study design, Trapani et al. (16) reported that JSLE children (N = 20) had the same BMD values when compared with a control group at baseline and after a one-year follow-up. Only in those patients aged 19 to 25 years was BMD significantly lower than in controls. However, the authors demonstrated that the mean yearly BMD loss in the steroid-treated patients was 0.031 g/cm^2 (3.5%) *vs* 0.005 g/cm^2 (0.5%) in those who had not taken steroids.

Peak bone mass plays an important role

Table 1. Demographic, anthropometric and clinical characteristics and bone mineral density (BMD) of patients with juvenile systemic lupus erythematosus (JSLE) and controls.

	JSLE patients	Control
Age (years)	13.3 ± 3.1	13.0 ± 3.0
Weight (kg)	37.3 ± 9.5	42.8 ± 10.6
Height (cm)	140.7 ± 13.1*	150.5 ± 12.3
Disease duration (years)	3.9 ± 2.7	-
Disease activity (SLEDAI)	7.7	-
Daily steroid doses (mg kg^{-1} day^{-1})	0.54 ± 0.42	-
Cumulative steroid doses (g)	14.2 ± 11.3	-
BMD (g/cm^2)	0.846 ± 0.199	0.946 ± 0.197

Data are reported as means ± SD for 16 patients and 32 controls. SLEDAI = systemic lupus erythematosus disease activity index.
*P = 0.01 compared to control group (Student *t*-test).

in determining the risk of developing osteoporotic fractures in adulthood. Since most bone mass is acquired during the pre- and perimenarcheal period, the importance of such event in growing girls should not be undervalued (23,24). During puberty, the total increase in BMD is higher than that during the preceding 10 years. The most important increase in lumbar spine BMD was found in pubertal stage 4 for girls and boys (12). It is during this stage of puberty that deceleration of the growth spur occurs and adult levels of sex steroids can be attained (12). In our study, we did not find a significant correlation between bone loss and pubertal stage. However, JSLE patients who were in stages G1-G2 presented lower BMD than patients in stages G3-G5. Our results indicated some increment in bone mass as a function of pubertal development even in patients with an important reduction in bone density.

We showed that weight is significantly correlated with BMD in JSLE, in agreement with other studies showing that weight is the best predictor of bone mass in healthy children (25,26).

Duration of disease was not related to BMD, as previously demonstrated in adult patients with SLE (22). However, there are many disease-related variables that could play a role in determining BMD in patients with JSLE (27-30).

Disease activity and steroid treatment did not correlate with BMD values in these patients. A larger number of patients would be required to support a statistically significant reduction in BMD.

Acknowledgments

We wish to express our thanks to Prof. Clovis de Araujo Peres and Prof. Fabio Tadeu Montesano for statistical assistance.

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