Bone Mineral Density Measured by Dual X-Ray Absorptiometry in Spanish Patients with Insulin-Dependent Diabetes Mellitus*

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Received: 14 August 1995 / Accepted: 16 November 1995

Abstract. Previous studies suggest that low bone mass is a potential complication of insulin-dependent diabetes mellitus. Nevertheless, the factors that influence diabetic osteopenia are not well established. In order to evaluate the prevalence and magnitude of diabetic osteopenia and its association with clinical and metabolic variables, we studied 94 consecutive patients with insulin-dependent diabetes mellitus. Their age ranged from 20 to 56 years and duration of diabetes varied from 1 to 35 years. Bone mineral density (BMD) was measured by dual X-ray absorptiometry at lumbar spine and proximal femur and the values were expressed as Z-score. The presence and extent of microvascular complications, degree of metabolic control, and other risk factors for osteoporosis were recorded and some biochemical markers of bone metabolism were assessed. Diabetic patients showed reduced BMD in all sites (lumbar spine: -0.89 ± 1.21; femoral neck: -0.99 ± 1.24; Ward triangle: -1.05 ± 1.24; P < 0.0001). Of the 94 patients 19.1% met diagnostic criteria for osteoporosis. BMD correlated with body mass index in all sites and with the duration of disease in Ward’s triangle. Presence and extent of diabetic complications were associated with lower BMD, as was smoking. No correlation was found between BMD and biochemical markers. In conclusion, osteopenia is a common complication in patients with insulin-dependent diabetes mellitus. Microvascular complications are a critical point in the progression of diabetic osteopenia. Other risk factors for osteoporosis (nutritional status and smoking) must be taken into account.

Key words: Insulin-dependent diabetes mellitus — Bone mineral density — Dual X-ray absorptiometry — Bone turnover markers — Microvascular complications.

Although osteopenia is not generally regarded as one of the major complications of diabetes mellitus, there is some evidence that diabetic patients have lower bone mineral density (BMD) than normal subjects [1–4]. However, the relationship between insulin-dependent diabetes mellitus (IDDM) and reduced BMD is not well established. Several pathogenic possibilities have been proposed such as bone microangiopathy [5, 6], insulinopenia [7], impaired regulation of mineral metabolism [8, 9], alterations in local factors that regulate bone remodeling [10], and even an intrinsic disorder associated with IDDM [11]. However, the complete picture of the pathogenesis of diabetic bone disease is still unknown and it has become clear that no single mechanism can explain all the observed phenomena.

A significant reduction in BMD has been reported in clinical studies using single photon absorptiometry [12–14], but in the few studies carried out by dual X-ray absorptiometry (DXA) there are conflicting results [15–17]. Moreover, the presence, extent, and localization of diabetic osteopenia are not well established. Furthermore, the influence of sex, duration of disease, degree of metabolic control, insulinization level, nutritional status, risk factors for osteoporosis, as well as long-term microvascular complications is largely unknown.

The aim of the current study was to evaluate the BMD at lumbar spine (LS) and proximal femur by DXA in IDDM patients and to analyze its possible relationship with a set of clinical and metabolic variables.

Patients and Methods

We studied 94 consecutive outpatients (45 males, 49 females) with IDDM defined in accordance with the criteria of the World Health Organization (WHO) [18] who attended the diabetic clinic. Their age ranged from 20 to 56 years (mean ± SD, 30 ± 9 years). The mean body mass index was 23.9 ± 3.8 kg/m². The duration of disease varied from 1 to 35 years (12 ± 8 years) and the insulin dose from 23 to 78 UI/day (42 ± 9 UI/day). Metabolic control was assessed by glycosilated hemoglobin (HbA₁c) measurements (automated high performance technique, Kyoto Domchi kagaku, Japan). The normal range for HbA₁c in our laboratory was 3.9–6.0%. The mean HbA₁c for the last year (three to four determinations) was calculated for each patient and this value was used for statistical analysis (8.5 ± 1.8%, range 4.6–13.0%).

The presence of chronic complications of diabetes was evaluated. Ophthalmologic exploration was performed using funduscopy and retinal fluorescein angiography and then the patients were placed into three groups: no retinopathy, background/preproliferative retinopathy, and proliferative retinopathy. Diabetic nephropathy was assessed by repeated determinations of 24-hour urine microalbuminuria, measured by immunoturbidimetry, and then the patients were divided into three groups: no nephropathy (UALB < 30 mg/day), microalbuminuria/preclinical nephropathy (UALB between 30–300 mg/day) and overt nephropathy (UALB > 300 mg/day). Patients with creatinine levels greater than
220 μmol/liter were excluded. The presence of peripheral or autonomic neuropathy were analyzed by clinical history and physical examination.

All women were premenopausal and eumenorrheic at the time of the study. Furthermore, none of the diabetic patients suffered from any other medical condition or were taking any medication thought likely to interfere with their bone metabolism. Alcohol consumption was not excessive (<40 g/day) and all had an appropriate degree of both physical activity and daily calcium intake.

The BMD was assessed by dual X-ray absorptiometry (Hologic QDR1000, Hologic Inc., Waltham, MA, USA). Measurements were made of the usual L2-L4 area at the LS, femoral neck (FN), and Ward’s triangle (WT). The values were expressed as z-score (number of SD adjusted by age and sex) in comparison with a reference healthy Spanish population (1221 males and 1331 females) [19]. The precision of measurement with repositioning was <2% for both spine and proximal femur BMD. Osteoporosis was defined as a value for BMD 2.5 SD or more below the young adult mean at spine or proximal femur according to recent WHO criteria [20].

Fasting morning blood samples were drawn for determinations of serum concentrations of calcium, phosphorus, creatinine, alkaline phosphatase, and tartrate-resistant acid phosphatase using an autoanalyzer (Hitachi 704 autoanalyzer, Tokyo, Japan). Intact parathyroid hormone (PTH-I) (IRMA, Incstar, Stilwater, MN, USA) and osteocalcin (BGP) (RIA, Incstar, Stillwater, MN, USA) were determined using commercial kits.

The results were expressed as mean ± standard deviation (SD) except when indicated. One sample t-test was used to assess the difference between the mean BMD z-score at each site and zero. The significance of the difference between groups was determined with analysis of variance. A linear correlation test was used to determine the relationship between BMD values and other variables. A probability of P < 0.05 was taken to indicate significant differences.

Results

The BMD values expressed as z-score were lower in diabetic patients when compared to reference standards in all sites (LS: −0.89 ± 1.21; FN: −0.99 ± 1.24; TW: −1.05 ± 1.24; P < 0.0001). The percentages of the BMD decrease in different sites were LS 9.1%, FN 12.0%, and WT 16.3%. No significant differences were found for comparing BMD between the measurement sites. Eighteen diabetic patients (19.1%) were considered to be osteoporotic; 9 men and 9 women. Male patients showed a lower BMD than female at the lumbar spine (−1.17 ± 1.04 versus −0.64 ± 1.30; P < 0.05) but no difference was found in the FN or the WT. A weak negative correlation was found between the duration of diabetes and the BMD (z-score) in the Ward’s triangle (r = −0.315; P < 0.002). No correlation was found between mean HbA1c levels and the BMD in any region. The body mass index had a direct correlation with the BMD in any region. Between mean HbAlc levels and the BMD in any region. The insulin dose (U/day) and the BMD (z-score) in the Ward’s triangle (r = −0.315; P < 0.002) but no difference was found in the FN or the WT.

Thirty-six (38%) diabetic patients had some degree of chronic diabetic complications; 31 presented retinopathy, 19 had nephropathy, and 9 had neuropathy. According to predefined criteria, we calculated the mean z-score values in subgroups of patients with retinopathy and nephropathy. Overall, patients with more advanced complications showed lower BMD. These results are presented in Figures 1 and 2. Patients with autonomic or peripheral neuropathy also showed lower BMD values. Diabetic patients who smoked (41/94) had a lower BMD than nonsmokers in FN (−1.29 ± 1.02 versus 0.76 ± 1.23; P < 0.04) and TW (−1.35 ± 1.15 versus −0.81 ± 1.16; P < 0.03).

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Mean values of serum calcium, phosphorus, alkaline phosphatase, tartrate-resistant acid phosphatase, BGP, and PTH-I were all found to be in normal range according to our laboratory (Table 1) and no correlations were found between biochemical markers and BMD measurements.

Discussion

Our results highlight the magnitude of diabetic osteopenia, thanks to the significant advances that the DXA offers in the assessment of BMD [21]. Hence, approximately 20% of the study population met diagnostic criteria of osteoporosis according to the new definition established by WHO [20], and both types of bone (cortical and trabecular) were similarly affected. Our findings contrast with previous reports [15, 16, 22] which showed minor changes in BMD. Such controversial data could be explained because of differences in the clinical profile of our patients: longer duration of diabetes, lower body weight, prevalence of risk factors for...