Internal Medicine - Pediatrics

Original Papers

Correlation between Adiponectin, Leptin, Insulin Growth Factor-1 and Bone Mineral Density in Pre and Postmenopausal Women

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Correlation between Adiponectin, Leptin, Insulin Growth Factor-1 and Bone Mineral Density in Pre and Postmenopausal Women (Abstract): Body weight positively correlates with bone mass, gravity being a stimulating bone stress. Adipose tissues could influence bone metabolism especially in postmenopause. Also, muscle mass positively correlates with bone mass and is dependent on physical activity, but also on some hormones with direct effect on bone, such as insulin growth factor-1 (IGF-1). Aim: Our study investigated the relative influence on lumbar bone mass of pre and postmenopausal women of body weight, leptin, adiponectin and IGF-1. Material and methods: Cross-sectional study including six groups of 8 to 15 pre and postmenopausal healthy volunteers with different weight; body mass index (BMI): normal and underweight (BMI<25 kg/m²), overweight (BMI 25-30 kg/m²), and obese (BMI>30 kg/m²). Lumbar bone mineral density (BMD) and body composition (BC) were evaluated by dual X ray absorptiometry (DXA, Hologic), while serum leptin, adiponectin and IGF-1 were measured by ELISA. Results: Body weight, fat and lean mass positively correlated with BMD, irrespective of age (p<0.05, ANOVA). Leptin was an independent predictor for bone mass only in postmenopausal women (p<0.05). Adiponectin negatively correlated (R²=0.1975) and IGF-1 positively correlated with body mass (p<0.05). Conclusions: Increased body weight prevents bone loss after menopause. Leptin and IGF-1 have adjacent positive roles in preserving bone mass during postmenopause. Key words: BODY COMPOSITION, LEPTIN, ADIPONECTIN, IGF-1, MENOPAUSE.

In recent years, many studies have been published showing the link between bone mass, body composition, and hormonal parameters. Their conclusions are: body weight has an important predictive effect on bone mass; body weight influences bone mineral density through both fat mass and lean mass; fat mass acts through several mechanisms, once through the pressure it exerts on the skeleton, then by its association with bone active hormones secretion, estrogen and leptin secretion by adipocytes (1), muscle mass is dependent not only on physical activity but also on hormones, such as IGF-1 and testosterone, that have a direct effect on bone (2).

Material and Methods
Cross-sectional study on 6 groups of about 8 women each. Age distribution: 31
premenopausal women and 37 postmenopausal women (at least two years of menopause). BMI: normal and underweight (BMI < 25 kg/m²), overweight (BMI 25-30 kg/m²) and obese (BMI > 30-40 kg/m²). Age-group and BMI distribution: premenopausal women: 16 normal weight and underweight, 9 overweight and 6 obese; postmenopausal women: 8 normal weight and underweight, 11 overweight and 17 obese. All women volunteered to participate in this study, and were recruited into the study from patients, students and staff of Iasi County „St. Spiridon” Emergency Hospital. A signed informed consent was obtained from all women.

Exclusion criteria were: diabetes mellitus, osteoporosis under treatment, hormone replacement therapy, severe liver or kidney disease, hyperthyroidism, primary hyperparathyroidism, hypogonadism, growth hormone deficiency, Cushing's syndrome, corticotherapy for over a year, anorexia nervosa, malabsorption syndrome, genetic syndromes. A fasting blood sample was collected, centrifuged, and stored in a refrigerator (-30°C) for estrone and estradiol determinations. Then, all volunteers’ height and weight were measured, and subjected to osteodensitometry by dual X-ray absorptiometry (DXA). A certified technician measured bone mineral density (BMD) of the lumbar spine on Hologic DXA. Total fat and lean masses were expressed in grams. Lumbar BMD was expressed in g/cm². Leptin (ng/ml), adiponectin (mg/l), IGF-1(μg/l) were determined using commercial ELISA kits (Diagnostic Automation Inc., Calabasas, CA). The results were statistically processed using NCSS 2007 software, simple Pearson correlation, student t test, the correlation being considered significant when p<0.05. Multivariate regression (ANOVA) was used to exclude systematic biases.

RESULTS

Lumbar BMD was significantly lower in all postmenopausal women regardless of body weight compared with premenopausal women (p<0.05). We found that lumbar mineral density in obese postmenopausal women was similar to that in obese premenopausal women, while normal weight or underweight postmenopausal women had a significantly lower BMD than premenopausal women (p<0.05) (fig. 1).

Fig. 1. Mean lumbar bone mineral density of premenopausal (left) and postmenopausal (right) women
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BMD in lean postmenopausal women was significantly lower than in premenopausal women (p<0.05). BMD in obese postmenopausal women was comparable to that of premenopausal women.

Body weight, expressed as BMI (kg/m^2), positively correlated with lumbar BMD, Z score for all women (fig. 2).

Leptin positively correlated with fat mass, while between leptin and Z score there was a significant correlation in all study groups, suggesting that leptin itself may have direct effect on bone (p<0.05, fig. 3).

IGF-1 correlated positively with bone mineral density in premenopausal women (r^2=0.1854, p<0.05), while adiponectin correlated negatively (r^2=0.1975) (fig. 4, 5).

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DISCUSSION

One factor correlated positively to bone mineral density is body weight. This can be explained by the mass effect, gravitational stress stimulating bone formation (3). Not completely elucidated is the relative importance of various body compartments, which may influence bone acquisition by mechanisms other than mechanical stress. Body weight is the sum of lean mass to fat mass. Increased muscle mass, combined with physical exercise, may contribute to a higher bone mass at young ages (4). Muscle mass is dependent not only on physical activity but also on hormones that have a direct effect on bone, such as IGF1 and testosterone (5). We demonstrated that IGF1 level positively correlates with bone mass (fig. 4), thus partially explaining the correlation between lean mass (source of IGF1 synthesis) of and bone mass. Low IGF1 level is considered by other authors to be predictive of low bone mass and osteoporosis (6).

Adipocyte secretes specific peptide hormones, called adipocytokine (7). Leptin is considered to be a mediator between adipocytes and bone metabolism. Osteoblasts have leptin receptors, which stimulate bone formation through a direct mechanism, but inhibit the recruitment of osteoclast precursors, reducing osteolysis (8). However, by central effect, leptin stimulates the sympathetic nervous system leading to bone demineralization. The literature on the role of leptin on bone are conflicting, some authors describing a positive predictive role, while others suggest either the loss of leptin influence on bone when normalized in adipose tissue, or a negative predictive role in some populations (9, 10).

In vitro and on animal models, adiponectin
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seems to have direct effects mediated by receptors located on osteoblast, determining an increased bone turnover with predominance of osteoclast activity, possibly associated to bone mass loss (11). The effects observed in vitro and on animal models have been confirmed by some studies (12). In agreement with these studies, we found a negative correlation of adiponectin with bone mass.

CONCLUSIONS
We have demonstrated that the various body compartments influence bone mass acquisition in different ways, mass effect-independent mechanisms included. Thus, lean tissue mass has a more important predictive role on bone mass than fat tissue mass or total body weight. This effect could be explained by a hormonal profile favoring muscle development and collagen matrix, such as higher levels of IGF1.

Adipokine secretion profile has a buffer effect, adiponectin being a negative predictor of bone mass acquisition.

Maintaining acceptable bone mass in postmenopausal women is essentially influenced by premenopausal bone mass acquisition, which depends on weight, lean mass, estrogen impregnation, and IGF1 levels as positive factors, but also on adiponectin as possible adverse prognostic factor.

REFERENCES