Saturday May 13, 2000 Lectures

Osteoporosis

PATHOPHYSIOLOGY OF OSTEOPOROSIS: MOLECULAR AND CELLULAR ASPECTS

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Osteoporosis must be viewed as a pathological condition which affects the entire skeleton and is characterized by a low bone mass in combination with microarchitecture changes particulary of cancellous bone, both adding to the fragility of bone at distinct sites of the axial as well as perpendicular skeleton. The two major determinants of bone mass and mineral density in later life in both sexes are (i) the extent of the peak bone mass in early adulthood as well as (ii) the rate of involutional bone loss thereafter, and are both governed by a complex interaction of genetic, age-related, hormonal, nutritional, environmental and life style factors in the regulation of systemic calcium and phosphate homeostasis and, equally important, of local bone remodeling processes. This lecture therefore will focus on some of the most recent findings in molecular and cellular biology of nuclear receptor-mediated actions of the steroid/vitamin D/thyroid hormones on osteoclast and osteoblast differentiation and function, and critically review their significance for etiology and pathogenesis of osteoporosis in men and women.

BONE MINERAL DENSITY IN INFLAMMATORY RHEUMATIC DISEASES.

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Secondary osteoporosis in patients with rheumatic diseases has been described for many years, mainly in rheumatoid arthritis, systemic lupus erythematosus and ankylosing spondylitis. However, data on bone mineral density (BMD) of other inflammatory rheumatic diseases are still missing.

Methods: BMD of the lumbar spine (L2-4) and femoral neck (FN) was measured by DXA densitometer NORLAND XR-26 in a group of 316 patients (276 women and 40 men) with 9 different inflammatory diseases (RA, JCA, SLE, SD, MCTD, AS, PA, PM, Sjogren's syndroma). BMD was compared with the reference values of the device (Z-score) and with the control group of Slovak EPOS centre comprising 367 probands using WHO diagnostic criteria for osteoporosis.

Results: In all the group, the average value of Z-score was significantly decreased in L2-4 (Z= -0,90) as well as in FN (Z= -0,95) areas. The lowest average Z-score was observed in AS patients (-l,63 and –2,12). On the other hand patients with Sjogren's syndroma had no significant decrease of BMD and patients with psoriatic arthritis had decrease of BMD only in femoral neck (Z-score= -0,88). Decrease of Z-score was significant in the other disease for spine and neck: RA (-0,97, -0,89), SLE (-0,65, -0,75), MCTD (-0,94, -l,l4), PM (-0,89, -0,90), SD (-l,21, -l,l8), JCA (-l,60, -l,36).

In patients over 50 years, incidence of OP was almost 50% in L2-4 and 35% in FN areas. In the group of postmenopausal patients, OP was found in L2-4 in as much as 46% and in FN area in 28% females compared to EPOS control group, while normal BMD values in L2-4 were observed only in 15% and in FN in 17,4% females.

Conclusion: Patients with inflammatory rheumatic diseases have high prevalence of osteoporosis in spine and femoral neck and their bone mineral density is about 1 SD lower than density of normal population.

BONE METABOLISM IN ANKYLOSING SPONDYLITIS

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Objective: to assess markers of bone formation and bone resorption in patients with ankylosing spondylitis.

Material and methods: Serum was obtained for measurement of bone alkaline phosphatase (BAP) by ELISA method from 44 male patients with AS aged 23-68 years and from 18 healthy male controls aged 21-66 years. We also measured fasting 2-h hydroxyproline/creatinine urinary ratio and calcium/hydroxyproline urinary ratio in 46 patients with AS aged 23-68 years and in 10 healthy male controls aged 25-69 years. We assessed activity of the disease by erythrocyte sedimentation rate (ESR), levels of fibrinogen, mucoproteids and C-reactive protein (CRP). We measured bone mineral density (BMD) at lumbar spine (LS), femoral neck (FN) and radius (R) by DEXA method.

Results: AS patients had lower BAP concentrations then control group (13,29 U/L v 15,77 U/L p=0,05). There was no correlation between activity of BAP and age and disease duration. There was also no correlation between activity of BAP and activity of the disease measured with ESR, CRP, fibrinogen and mucoproteids. AS patients had increased hydroxyproline excretion with urine measured with hydroxyproline/creatinine index when compared with control group (0,017 v 0,011, p=0,02). There was no correlation between hydroxyproline/creatinine index and age and disease duration. There was also no correlation between hydroxyproline/creatinine index and activity of the disease measured with ESR, CRP, fibrinogen and mucoproteids. There was no difference in excretion of calcium between AS patients and control group. Among parameters of BMD at different sites of skeleton we found only positive correlation between BMD at LS and activity of BAP.

Conclusion: Patients with AS have decreased bone formation and increased bone resorption measured with BAP and hydroxyproline/creatinine ratio.

BONE CHANGES IN GASTROINTESTINAL DISEASES

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Gastrointestinal (GIT) diseases are a common, cause of metabolic bone changes.

The aim of the study was to indicate GIT diseases (lactose intolerance, non-lactose intolerance, Crohn's disease, ulcerative colitis, pancreatic insufficiency, states after gastric resection, chronic diseases of the liver, and coeliac disease) by means of literature data and the authors' own results coinciding with the detected low bone density and thus increased risk of fracture. In our studies in patients suffering from chronic pancreatitis (n=34), ulcerative colitis (n=25) and liver cirrhosis (n=36},

a significant decrease of bone mass density was observed. Bone changes coinciding with GIT diseases are frequent and are commonly asymptomatic for a long period. Conclusion: In coincidence with GIT diseases the authors indicate the necessity of being aware of the risk of bone changes development and to investigate them actively. An early diagnosis aids to introduce preventive and therapeutical measures and to halt or at least slow down the origin of bone changes.

BONE DENSITOMETRY AND ITS ROLE IN CLINICAL DECISION MAKING.

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A number of densitometric techniques are now widely used in clinical practice to predict fracture risk in individuals with clinical risk factors. At present, dual-energy X-ray absorptiometry /DXA/ is regarded as the best method for use in clinical practice, both for predicting fracture risk and for monitoring the effect of treatment. In our center we have performed since 1993 more than 25 000 scans using DXA /Norland XR 36, USA/. A measurement of lumbar spine and hip are routinely made in each patient, because the bone loss in osteoporosis may be heterogeneous and there is sometimes discrepancy between the level of BMD at these two sites. The diagnosis of osteoporosis may be missed if only one site is measured. However spinal measurement become unreliable in later life the presence of osteophytes, extraskeletal calcifications and vertebral deformities, all of which may rise artifactually the BMD value. It still remains debate on, how the results obtained should be used to make decision about treatment. Extrapolation of diagnostic criteria to interventional thresholds is a key issue in clinical decision making. Clearly, factors other than BMD may influence treatment decision. The presence of other risk factors for fracture /unrelated to BMD/, age, gender, relevant medical comorbidity and risk/benefit ratio and the cost of the treatment proposed are very important factors too. Therefore, correctly identifying those women at highest risk for developing fractures will be extremely useful in helping them make a rational and informed decision about intervention with pharmaceutical agents.