Determinants of peak bone mass

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At a given age, bone mass, which is a predictor of fracture risk, is determined by the amount of bone accumulated at the end of the period of skeletal growth, the so-called peak bone mass, and by the amount of bone lost subsequently, particularly during the last third of life. Thus, peak bone mass is a significant determinant of fracture risk later in life. There is no difference in areal bone mineral density (aBMD), which is a surrogate evaluation of bone mass and captures a component of bone size, or in volumetric bone density, the amount of bone in bone, at birth between male and female before puberty. During puberty, bone mass more than doubles. A gender difference begins to be expressed in males as a consequence of a more prolonged growth period, and of a peak of bone growth velocity slightly, but not significantly higher. Thus, males are accumulating more bone, mostly by greater bone size development. A late menarche is associated with a lower aBMD and a higher risk of fracture later in life. Peak bone mass is achieved for most parts of the skeleton by the end of the second decade. The factors contributing to the large variance in bone mass at that time are genetics, race, gender, dietary intakes, endocrine factors, mechanical forces, or the exposure to deleterious influences. Genetics appear to be the most important one, accounting for more than 70% of the variance. This genetic influence is detectable well before puberty with bone growth following a track throughout puberty. Nutritional intakes are able to modulate this genetic potential, with effects starting as early as in utero. A lower femoral neck aBMD has been recorded in prepubertal former preterm girls. Furthermore, prepubertal girls seem to express benefits in bone mass long after the cessation of vitamin D supplements during the first year of life. Calcium supplementation favorably influences bone mineral mass accumulation, particularly in the peripheral skeleton. The positive response to calcium supplements may mostly be detected in a given vitamin D receptor genotype. Calcium supplements in prepubertal girls appear to hasten the occurrence of menarche. When aBMD is measured more than 7 years after cessation of calcium supplementation, a persistent effect of the latter is detectable in those girls with an earlier menarche. Boys peripheral skeleton is also responsive to calcium supplements. Protein intakes in children and adolescents are susceptible to influence bone growth and bone mass accumulation through mechanisms likely to involve IGF-I secretion and action. IGF-I is an essential factor for longitudinal bone growth, as it stimulates proliferation and differentiation of chondrocytes in epiphyseal plate. IGF-I also plays a role in trabecular and cortical bone formation. Thus, IGF-I can exert anabolic effects on bone mass not only during growth, but also during adulthood. Furthermore, by its renal action on tubular reabsorption of phosphate and on the synthesis of calcitriol, through a direct action on renal cells, IGF-I can be considered as an important controller of the intestinal absorption and of the extracellular concentration of both calcium and phosphate, the main elements of bone mineral. Furthermore, it could be directly implicated in bone matrix mineralization, as shown in osteoblast-specific IGF-I receptor knockout model. In adolescents, the peak of high longitudinal growth precedes by one to two years the peak in bone mineral mass accrual during pubertal spurt, highlighting some interaction with other factors in determining longitudinal growth and bone mass accumulation.

The hepatic production and plasma levels of IGF-I are under the influence of dietary proteins. Protein restriction has been shown to reduce IGF-I plasma levels by inducing a resistance to the action of GH at the hepatic level, and by an increase of IGF-I metabolic clearance rate. Decreased levels of IGF-I are found in states of undernutrition such as marasmus, anorexia nervosa, celiac disease or HIV infected patients. Refeeding these patients led to an increase of IGF-I. Furthermore, elevated protein intake is able to prevent the decrease in IGF-I usually observed in hypocaloric state. In addition, protein restriction could render target organs less sensitive to IGF-I. When IGF-I is given to rats maintained under a low protein diet at doses normalizing their plasma levels, it fails to restore skeletal growth and/or bone formation. When growth hormone is administered to rats fed an isocaloric low protein diet, there is even a significant decrease in bone strength. Furthermore, protein intakes could modulate the response to calcium supple-
ments. Indeed, in prepubertal boys, the favorable effects of calcium supplements are mostly detectable in those with a lower protein intake.

Various disorders can impair optimal bone mass acquisition during childhood and adolescence. In some disorders, such as Turner’s syndrome, Klinefelter’s syndrome, glucocorticoid excess, hyperthyroidism or growth hormone deficiency, low bone mass has been attributed to abnormalities in a single hormone. In diseases such as anorexia nervosa and exercise-associated amenorrhea, malnutrition, sex steroid deficiency and other factors combine to increase the risk of osteopenia or low bone mass.

Environmental factors seem to affect bone accumulation at specific times during infancy and adolescence, and maybe in a skeletal site-specific way. Optimization of peak bone mass through a favorable conjunction of environmental factors could be considered as an efficacious long-term prevention of osteoporosis in the elderly.

BIBLIOGRAPHY


