Endocr Rev. 2004 Jun;25(3):389-425.

Androgens and bone.

Vanderschueren D, Vandenput L, Boonen S, Lindberg MK, Bouillon R, Ohlsson C.

Source

Laboratory for Experimental Medicine and Endocrinology, Katholieke Universiteit Leuven, Leuven, Belgium.

Abstract

Loss of estrogens or androgens increases the rate of bone remodeling by removing restraining effects on osteoblastogenesis and osteoclastogenesis, and also causes a focal imbalance between resorption and formation by prolonging the lifespan of osteoclasts and shortening the lifespan of osteoblasts. Conversely, androgens, as well as estrogens, maintain cancellous bone mass and integrity, regardless of age or sex. Although androgens, via the androgen receptor (AR), and estrogens, via the estrogen receptors (ERs), can exert these effects, their relative contribution remains uncertain. Recent studies suggest that androgen action on cancellous bone depends on (local) aromatization of androgens into estrogens. However, at least in rodents, androgen action on cancellous bone can be directly mediated via AR activation, even in the absence of ERs. Androgens also increase cortical bone size via stimulation of both longitudinal and radial growth. First, androgens, like estrogens, have a biphasic effect on endochondral bone formation: at the start of puberty, sex steroids stimulate endochondral bone formation, whereas they induce epiphyseal closure at the end of puberty. Androgen action on the growth plate is, however, clearly mediated via aromatization in estrogens and interaction with ERalpha. Androgens increase radial growth, whereas estrogens decrease periosteal bone formation. This effect of androgens may be important because bone strength in males seems to be determined by relatively higher periosteal bone formation and, therefore, greater bone dimensions, relative to muscle mass at older age. Experiments in mice again suggest that both the AR and ERalpha pathways are involved in androgen action on radial bone growth. ERbeta may mediate growth-limiting effects of estrogens in the female but does not seem to be involved in the regulation of bone size in males. In conclusion, androgens may protect men against osteoporosis via maintenance of cancellous bone mass and expansion of cortical bone. Such androgen action on bone is mediated by the AR and ERalpha.