

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Overexpression of osteoprotegerin suppressed bone resorption and increased vertebral bone volume, density, and strength

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Osteoporosis is characterized by a progressive reduction of bone mass which usually results from an imbalance between bone formation and bone resorption. Osteoclastogenesis is a tightly regulated process. A crucial step of osteoclast formation is the binding of RANKL (Receptor Activating NFκB Ligand) on its receptor RANK in osteoclast precursors. Osteoprotegerin (OPG) is a decoy RANK receptor which binds RANKL thereby preventing its interaction with RANK. Therefore, OPG reduces osteoclast differentiation and bone resorption, and has emerged as a potential treatment for osteoporosis. Indeed, transgenic mice overexpressing OPG have increased bone mass. However, long-term effects of osteoprotegerin expression on bone biomechanical properties and health have not been studied so far.

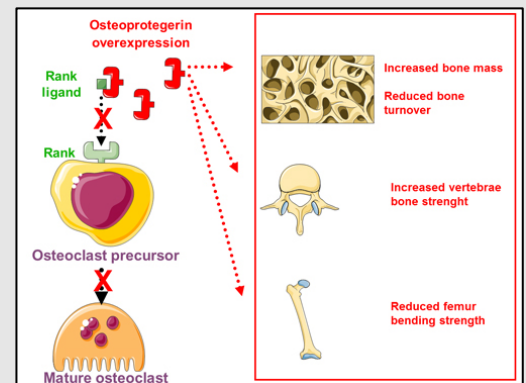
To assess this issue, Ominsky et al. generated transgenic rats overexpressing OPG under the control of a liver-specific promoter and analyzed their phenotype 1 year after birth [1]. Transgenic and wild type animals did not differ in terms of weight, height, red blood cell count, creatinine, calcium, and phosphorus serum levels. Osteoprotegerin overexpression was not associated with skeletal fractures or impaired tooth eruption. The authors further characterized bone structure and mechanical properties of vertebrae and femurs from transgenic and wild-type animals. Prolonged osteoprotegerin overexpression reduced bone turnover and increased bone mass in a dose-dependent manner, without affecting bone growth. Osteoprotegerin overexpression impact on bone mechanical properties differed between lumbar vertebrae and femur. The former showed increased bone strength while the latter had reduced bending strength. The reduction of femurs bending strength may be the consequence of the mild osteopetrotic changes induced by osteoprotegerin which include a reduction in periosteal perimeter.

This study demonstrates that the low bone turnover induced by osteoprotegerin overexpression leads to increased bone mass with no evidence for deleterious effects on bone material properties. The way osteoprotegerin chronic expression affects bone mechanical strength varied with bone type.

1. Ominsky MS et al. *J Bone Miner Res.* 2009;24:1234-1246.

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RANKL is a soluble molecule that binds to RANK, its receptor, in osteoclast precursors and induces osteoclast differentiation. Osteoprotegerin (OPG) is a decoy RANK receptor which binds RANKL and prevents its binding on RANK. Therefore OPG reduces osteoclast differentiation and bone resorption. Rats overexpressing osteoprotegerin have reduced osteoclast differentiation. After 1 year, this led to an increase in bone mass and a reduction of bone turnover but did not affect bone material properties. Osteoprotegerin overexpression increased lumbar vertebral bone strength but reduced femur bending strength.



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