

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

RANKL inhibition with osteoprotegerin increases bone strength in ovariectomized rats

N°92 – August 2009

Ovariectomy results in bone loss caused by increased bone resorption. RANKL is an essential mediator of bone resorption. The purpose of a recent study [1] was to examine whether the RANKL inhibitor osteoprotegerin (OPG) would preserve bone volume, density, and strength in ovariectomized rats. Rats were ovariectomized or sham-operated at 3 mo of age. Sham controls were treated for 6 wk with vehicle. Ovariectomized rats were treated with vehicle or human OPG-Fc (10 mg/kg, 2/wk). Serum RANKL and TRACP5b, an osteoclast marker, was measured by ELISA. BMD of lumbar vertebrae (L1–L5) and distal femur was measured by DXA. Right distal femurs were processed for bone histomorphometry. Left femurs and the fifth lumbar vertebra (L5) were analyzed by μ CT and biomechanical testing, and L6 was analyzed for ash weight.

Ovariectomy was associated with significantly greater serum RANKL and osteoclast surface and with reduced areal and volumetric BMD. OPG markedly reduced osteoclast surface and serum TRACP5b while completely preventing ovariectomy-associated bone loss in the lumbar vertebrae, distal femur, and femur neck. Vertebrae from OPG-administered rats had increased dry and ash weight, with no significant differences in tissue mineralization versus ovariectomized controls. μ CT showed that trabecular compartments in ovariectomized-OPG rats had significantly greater bone volume fraction, vBMD, bone area, trabecular thickness, and number, whereas their cortical compartments had significantly greater bone area. OPG improved cortical area in L5 and the femur neck to levels that were significantly greater than ovariectomized or sham controls. Biomechanical testing of L5 and femur necks showed significantly greater maximum load values in the ovariectomy-OPG group. Bone strength at both sites was linearly correlated with total bone area, which was also significantly increased by OPG.

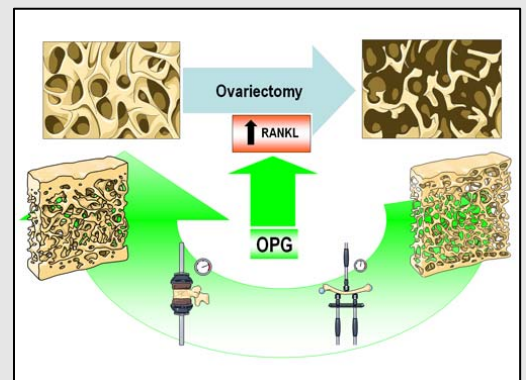
In conclusion, ovariectomy-related bone loss in rats was a RANKL-dependent event which can be efficiently blocked by OPG with preserved trabecular architecture, and increased cortical area and bone strength.

1. Ominsky M et al. *J Bone Miner Res.* 2008;23:672-682.

RANKL inhibition with osteoprotegerin increases bone strength by improving cortical and trabecular bone architecture in ovariectomized rats

Ovariectomy results in bone loss because of decreased bone formation and increased resorption. Increased production of RANK ligand (RANKL) stimulates osteoclasts. Administration of osteoprotegerin (OPG), a decoy receptor of RANKL, to ovariectomized rats restored bone mass. Both trabecular and cortical bone structure were improved. Biomechanical testing of vertebra and femur showed significantly greater maximum load values in the OPG-administered animals.

Ovariectomy-related bone loss in rats was a RANKL-dependent event which can be efficiently blocked by OPG with preserved trabecular architecture, and increased cortical area and bone strength.



PROTELOS[®]

Treatment of postmenopausal osteoporosis to reduce the risk of hip and vertebral fractures

SERVIER