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Skeletal deterioration induced by RANKL infusion

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RANK ligand (RANKL) is produced by osteoblasts and is an essential mediator for osteoclast development. No study has examined in detail the direct skeletal consequences of excess RANKL on bone turnover, mineralization, architecture, and vascular calcification. The authors of a recent study [1] administered soluble RANKL continuously to mature rats and created a bone-loss model. Six-month-old Sprague-Dawley rats were assigned to three groups (n=12) receiving continuous administration of saline (VEH) or human RANKL (35 µg/kg/day or 175 µg/kg/day) for 28 days. Blood was collected routinely during the study. At sacrifice, hind limbs and aorta were removed and samples were analyzed.

High-dose RANKL markedly stimulated serum osteocalcin and tartrate-resistant acid phosphatase (TRAP)-5b levels and reduced femur cortical bone volume (-7.6%) and trabecular volume fraction (BV/TV) at the proximal tibia (-64% vs VEH). Bone quality was significantly degraded in the high-dose group, as evidenced by decreased femoral percent mineralization, trabecular connectivity, and increased endocortical bone resorption parameters. Both cortical and trabecular bone mechanical properties were reduced by high-dose RANKL. No differences were observed in the mineral content of the abdominal aorta.

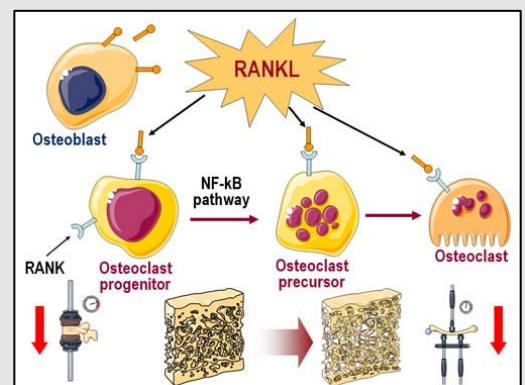
In conclusion, continuous RANKL infusion had detrimental effects on rat skeleton. These changes are comparable to those commonly observed in high-turnover bone diseases such as postmenopausal osteoporosis.

1. Yuan YY et al. *Osteoporos Int.* 2007;19:625-635.

Skeletal deterioration induced by RANKL infusion

Osteoclasts and their precursors bear a membrane receptor called RANK which activates the NF-κB signaling pathway and is instrumental in osteoclast differentiation. Activation occurs when the ligand of RANK is present. RANKL is synthesized by osteoblasts and mesenchymal stem cells. RANKL infusion in rats reduced cortical bone volume and trabecular volume fraction as well as bone quality and mineralization. As a consequence, both cortical and trabecular bone mechanical properties were reduced by high-dose RANKL infusion.

In conclusion, continuous RANKL infusion had detrimental effects on rat skeleton. These changes are comparable to those commonly observed in high-turnover bone diseases such as postmenopausal osteoporosis.



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