Enhancement of experimental fracture-healing by systemic administration of recombinant human parathyroid hormone (PTH 1-34).

BACKGROUND: Recombinant human parathyroid hormone (PTH [1-34]; teriparatide) is a new treatment for postmenopausal osteoporosis that can be systemically administered for the primary purpose of increasing bone formation. Because several studies have described the enhancement of fracture-healing and osteointegration in animals after use of PTH, we sought to critically analyze this skeletal effect. METHODS: Two hundred and seventy male Sprague-Dawley rats underwent standard, closed femoral fractures and were divided into three groups that were administered daily subcutaneous injections of 5 or 30 mug/kg of PTH (1-34) or vehicle (control). The dosing was administered for up to thirty-five days. Groups were further divided into three subgroups and were killed on day 21, 35, or 84 after the fracture. The bones were subjected to mechanical torsion testing, histomorphometric analysis, or microquantitative computed tomography. RESULTS: By day 21, calluses from the group treated with 30 mug of PTH showed significant increases over the controls with respect to torsional strength, stiffness, bone mineral content, bone mineral density, and cartilage volume. By day 35, both groups treated with PTH showed significant increases in bone mineral content and density and total osseous tissue volume, and they demonstrated significant decreases in void space and cartilage volume ($p < 0.05$). Torsional strength was significantly increased at this time-point in the group treated with 30 mug of PTH ($p < 0.05$). While dosing was discontinued on day 35, analyses performed after eighty-four days in the group treated with 30 mug of PTH showed sustained increases over the controls with respect to torsional strength and bone mineral density. No change was noted in osteoclast density at the time-points measured, suggesting that treatment with PTH enhanced bone formation but did not induce bone resorption. CONCLUSIONS: These data show that daily systemic administration of PTH (1-34) enhances fracture-healing by increasing bone mineral content and density and strength, and it produces a sustained anabolic effect throughout the remodeling phase of fracture-healing.