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Session: Osteoporosis Epidemiology: Bone Mineral Density

Presentation Number: W258

Title: Percutaneous Injection of Allantoin Accelerates Fracture Repair

Presentation Start: 9/19/2007 11:30:00 AM

Presentation End: 9/19/2007 2:30:00 PM

Category: P - Bone Biomechanics and Quality

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Allantoin is a botanical extract of the comfrey plant and is used for its healing, soothing, and anti-irritating properties. Allantoin helps to heal wounds and skin irritations and stimulate growth of healthy tissue. Its chemical formula is C4H6N4O3. It is also called 5-ureidohydantoin or glyoxyldiureide. In this study, we examined the effects of allantoin on the proliferation of the osteoblastic cell lines, MC3T3 and ROS17/2.8, in vitro; and on fracture repair in vivo. Cell cultures were treated with allantoin (1, 10 and 100 nM) for seven days (From Day 1 of culture to Day 7). On day 7, MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) and cell counting assays were performed to examine the effect of allantoin on osteoblast proliferation. Allantoin significantly induced osteoblast proliferation in a dose dependent manner as compared to control cultures (35% and 56% increase for 10 and 100 nM, respectively, $p<0.05$). It is important to mention that Carcinogenic Potency Project (CPP) studies demonstrated that allantoin has no carcinogenic effects on male or female rats and mice. We further examined the effect of allantoin on fracture repair. Experimental fractures were performed on 8-week Sprague-Dawley rats under anesthesia as follow: from an anterior incision we performed a transverse osteotomy at the mid tibia with a bone saw. The animals were then treated with vehicle or allantoin (weekly percutaneous injections;10 mg/Kg) for up to 4 weeks. Torsional biomechanical testing indicated that the stiffness of the allantoin-treated fractures was 2 fold higher than that of control groups at the two, three, and four-week time-points. The strength of the allantoin-treated fractures was 34%, 60% and 77% greater than that of controls at 2 ($p<0.05$), 3 ($p<0.005$) and 4 weeks ($p<0.005$), respectively. At 4 weeks, the stiffness and strength of the allantoin-treated fractures were equal to those of the intact contralateral tibia, whereas the buffer-treated and untreated fractures were significantly weaker than the intact tibiae. These data demonstrate that percutaneous injections of allantoin accelerate fracture repair in this fracture repair model. Our data on osteoblastic cell lines in-vitro suggest the possibility that the beneficial effects of allantoin on bone may result from increasing osteoblast proliferation and thereby bone formation at the fracture site.