Effects of parathyroid hormone treatment on distraction osteogenesis in the rabbit tibial lengthening model

Ramune Aleksyniene, MD

This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Aarhus, and defended on September 5 2008.

Official opponents: Bjarne Møller-Madsen, Klaus Hindsø, and Harald Steen, Norway.

Tutor: Ivan Hvid.

Correspondence: Ramune Aleksyniene, Ortopædkirurgien, Sdr. Skovvej 11, 9000 Aalborg. Denmark.

E-mail: raa@rn.dk

Dan Med Bull 2008;55:229

ABSTRACT

Parathyroid hormone (PTH), a peptide hormone consisting of 84 amino acids, is the principal regulator of calcium homeostasis and a key factor in the control of bone remodelling. Intermittently administered human PTH is a strong anabolic treatment regimen. Teriparatide, a recombinant form of the N-terminal of endogenous human PTH, has been available for clinical use for treatment of osteoporosis since 2002. In recent years the anabolic PTH effect on bone has evoked considerable interest within the orthopaedic field.

The present dissertation aimed to evaluate the effect of PTH on quality and strength of the newly regenerated bone formed during distraction osteogenesis in rabbits, the animals that have Haversian bone remodelling system similar to humans.

A total of 72 New Zealand white rabbits were used as a model for bone lengthening. They underwent right tibia lengthening by callus distraction using an external monolateral fixator. Prolonged bone samples underwent DEXA scanning, microcomputed tomography, additional callus volume was measured, and the destructive biomechanical three-point bending test was performed. Furthermore, we performed the DEXA analysis and the biomechanical three-point bending test of the contralateral non-operated tibia, and the bone-surrounded distracted callus was analysed by DEXA.

We found that intermittent treatment with PTH during distraction osteogenesis had a marked anabolic effect on newly regenerated bone. Intermittently administered PTH enhanced new bone formation and development, including the macro- and microstructure, DEXA-parameters and bone strength, of regenerated callus in rabbits. In addition, intermittent PTH treatment caused anabolic changes in the bone surrounding the distraction osteogenesis area proximal and distal to distracted callus. Moreover, PTH treatment enhanced bone mineral density and the mechanical strength of intact tibia bone in a time-dependent manner.

Although the scientific knowledge is at present very limited because very few experimental studies have been performed in this field, the present study does indicate that intermittent PTH treatment could be considered as a possible treatment regimen for bone stimulation in orthopaedic surgery, and that a positive anabolic effect on regenerate bone could be expected in humans.