7 SUMMARY

Histological, immuno-histological and histomorphometrical evaluation of the influence of systemically administered species-specific growth hormone on osteochondral defect healing in yucatan-minipigs

The aim of this study was to investigate if the application of species-specific growth hormone is capable of improving the quality of regenerative tissue during the early stages of osteochondral defect healing. An osteochondral defect (diameter 6 mm, 1 mm penetration into subchondral bone) was created in the proximal third of the left lateral femoral condyle in each of 54 mature female yucatan-minipigs. The animals were randomly divided into three groups with a postoperative healing time of four, six and twelve weeks. Half of the animals in each group received a daily injection of recombinant porcine growth hormone (100 μg/kg bodyweight). Gait analysis was performed on twelve pigs of the six and twelve week group at regular intervals throughout the healing period.

After sacrifice, all lateral femoral condyles were sawed in the sagittal plane, vertically halving the osteochondral defects. The lateral parts of all specimens were embedded in methylmethacrylate. Serial slices stained with Safranin-orange/von Kossa and Safranin-orange/fastgreen were analysed histomorphometrically, using a computerized image analysis system. In addition, histomorphometrical scores (O'Driscoll and Wakitani) were obtained. Immunohistochemistry was performed on the paraffin-embedded medial parts of the specimens with the following antibodies: anti-BMP-6, anti-IGF-I, anti-IGF-II, anti-IGF-I-receptor, anti-TGF-ß. Vessels were stained with anti-α smooth muscle actin.

Gait analysis showed a significant initial unloading of the hindlimb for approximately two weeks postoperatively, with all animals returning to normal loading shortly thereafter. The histomorphometrical analysis and scoring displayed an increase in the amounts of both new bone and cartilage over time. Similarly, the amounts of fibrous tissue and non-filled area decreased. In the six week group, significantly more bone and complete filling of the defect could be seen in the animals treated with growth hormone. All active types of cells, e.g. fibroblasts, osteo- and chondroblasts and their precursor cells were able to express all tested growth factors simultaneously. The numbers of each of these declined over time. Six weeks postoperatively, the animals treated with growth hormone, showed a lower vascular density than the animals treated with placebo.

The daily systemic application of species-specific growth hormone in a high dosage therefore seems capable of improving the initial process of regeneration of osteochondral defects. Compared to other studies, however, this osteochondral defect regeneration appears to be less effective. Considering the possible side effects and the costs of this form of treatment, the systemic administration of growth hormones for osteochondral defects appears unreasonable.