BONE DEFECT OSTEOSTEOINDUCTION BY TGF-BETA AND IGF-1 RELEASED FROM A BIODEGRADABLE OSTEOCONDUCTIVE HYDROGEL IN RAT TIBIA

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Introduction: The need for bone repair is one of the major concerns in reconstructive surgery. Bone defects are performed in order to repair congenital and acquired bone pathologies. To aid the healing process it is often necessary to induce osteogenic response in the healing tissue. Recently biodegradable hydrogels were shown to be promising biomaterial matrix for growth factors release (1). A study was made on the ability of TGF-β1, IGF-1 and of a combination of TGF-β1 and IGF-1 incorporated into acidic gelatin hydrogel to induce bone osteoinduction in a rat tibia defect model.

Experimental design: Segmental bone defects were performed in rat tibiae following induction of an external fixation device providing a rigid frame for the bone defect and hydrogels impregnated with growth factors were introduced at the defect site. Bone regeneration was assessed by soft tissue X-rays, axial and 3-D CT and by histology and SEM.

Materials and Methods: External fixation (EF) (2) was performed in 3-month-old Sprague-Dawley rats. Segmental bone defects (4mm) were induced by a micromotor between the two pins of the EF device (Figure 1). Hydrogels (95%wt), prepared by crosslinking of acid gelatin with glutaraldehyde and containing 0.1 µg TGF-β1, 25 ng IGF-1, 0.1 µg TGF-β1+25 ng IGF-1, saline, or hydrogel, were introduced into the defect. Radiologic soft tissue X-rays were performed on the day of operation and on 2, 4, 6 weeks postoperatively. Lower limbs were collected for general morphology, axial and 3-D CT, and for morphological analyses.

Results: Calcified material was observed following two weeks in defects that had been treated with TGF-β1. Morphology revealed that by this time the hydrogel was absent from the defect and that new bone formation was present in the margins of the defect. After four weeks, bone defects treated with TGF-β1, IGF-1 or TGF-β1+IGF-1 revealed radiopaque material in the defect region and by six weeks the amount of calcified material increased in TGF-β1 and TGF-β1+IGF-1 compared to hydrogel and to saline-containing hydrogel. CT axial radiology images revealed that following six weeks of treatment with TGF-β1 or TGF-β1+IGF-1, a solid bone was present in former sites of the defect. A less pronounced bone induction was observed in IGF-1-treated bones and control specimens revealed non-healing of the bone defect. 3-D CT (Figure 2) revealed that the bone had completely restored its three dimensional shape and that some overgrowth of regenerating bone was observed around the EF pins.

Conclusions: Acid gelatin hydrogel was shown to be a good osteoconductive matrix for growth factors (3). It increased the availability of growth factors in the site of bone healing and it also provided a space for bone regeneration. TGF-β1 and combinations of TGF-β1 and IGF-1 with hydrogel scaffold were shown to effective in osteoinduction (4), and can serve as good therapeutic agents for reconstruction of defects induced in long bones.

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