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The use of a bioresorbable calcium phosphate cement in partial tibial plateau defects in sheep

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Introduction

Synthetic bone replacements have been introduced in orthopaedic surgery in various formulations[1,7] with some of them based on natural sources, such as pretreated bovine bone matrix[2], or on synthetic source like hydroxyappatite[3] and tricalcium phosphates[12]. However, liquid bone cements that harden *in situ* and may be shaped according to the wishes of the surgeon are still quite rare. Hydaulic calcium phosphate cements (CPC) were recently described[5,6,9]. The end-product of the reaction is either brushite ($CaHPO_4 \cdot 2H_2O$) or an apatite (e.g. hydroxyapatite $Ca_5(PO_4)OH$) . Based on their solubility, brushite CPC are supposed to be far more resorbable than apatite cements. Several *in vivo* studies have shown indeed that brushite CPC are resorbable[5,6].

In this study, the behavior of two brushite cements was compared to a commercially available apatite cement in an experimental animal model in sheep.

Materials and Methods

The two brushite CPC (BC1[1] and BC3) were obtained from Dr h.c. Robert Mathys Foundation and Stratec Medical (Switzerland). These CPC are biphasic, i.e. they consist of fine brushite crystals and large granules of β-tricalcium phosphate (β-TCP; <0.5mm in diameter). The porosity of the matrix and the granules is close to 35%. BC1 has the same composition as BC3, except that it contains a larger β-TCP to monocalcium phosphate monohydrate ratio (2 instead of 1.27, in weight percent). The powder-to-granule ratio and the powder-to-liquid ratio are both equal to 2 (in weight percent). The liquid phase consists of a sodium hyaluronate solution.

A partial tibial plateau defect of 2.5 cm in depth and 1 cm heights at the anterior aspect of the tibial crest and an 8 mm drill defect in the distal femoral condyle was used as an experimental model in sheep. 16 sheep were divided in groups A and B. In group A , BC1 was used for the partial tibial plateau defect, whereas BC3 was applied in the drill hole of the femoral condyle. The tibial defect was stabilized by means of a 3.5 mm T-plate with screws. Animals were sacrificed 2, 4, 6 and 8 weeks, and 2, 4 and 6 months after surgery. Group B received a commercially available hydroxyapatite cement (Norian SRS, Norian Corporation, Cupertino, CA, USA) in both, the tibial and the femoral bone defects and served as controls. There, the animals were sacrificed 6 months after surgery.Radiographs were made immediately postoperatively and microradiographs at the time of sacrifice. The bones were harvested immediately after euthanasia. Macroscopic appearance of the defects was recorded, emphasizing tissue reaction of the environment, incorporation of the cement and if possible, the degree of cement resorption and new bone formation. Thereafter histology sections of undecalcified bone samples were prepared[4,8,11], where bone samples were embedded in acrylic resin. Grinding sections of 30-40 µm (Leitz Saw Microtome 1600) and thin sections of 5 µ stained with Toluidine blue or van Kossa/McNeal allowed microscopic analysis where cement resorption, new bone formation and cellular reaction were assessed. Histomorphometrical measurements (Leica, Qwin, Quips Program) were used to calculate the ratio of cement/ new bone according to the time of sacrifice.

Results and Discussion

Both types of CPC were well integrated within the original defect. The BC1 and BC3 were almost completely resorbed 6 months after surgery. In contrast, almost no bone resorption of the hydroxyapatite cement (Norian SRS) was visible at the same time period. At 2 months, about 25%, and at 4 months about 60% of the BC1 and BC3 was resorbed, while at the resorption front new bone formation was recorded. Although radiologically a small radiolucent zone could be demonstrated in some of the specimens, macroscopically and histologically this gap was not visible. Macroscopically, the cement seemed well incorporated at the bone periphery and no tissue reaction immediately adjacent to the bone cement was noted. Histologically, active bone resorption was demonstrated with osteoclasts directly at the cement surface digesting the original cement material. In the small interface between the new bone and the cement, multinuclear cells with incorporated cement material were seen, while new osteoid was deposited in the surface of TCP granules. TCP granules and the liquid cement phase were replaced by *creeping substitution*[10], which is the normal mechanism of bone replacement.

Conclusions

Overall, the brushite bone cements were well tolerated by the tissue, and resorbed much faster compared to the hydroxyapatite cement.

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