THE IMMEDIATE TISSUE REACTION TO A BIORESORBABLE BRUSHITE CEMENT IN EXPERIMENTAL METAPHYSEAL DEFECTS IN SHEEP

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INTRODUCTION: Resorbable cements as synthetic bone replacement have been introduced into orthopedic surgery for various applications, such as bone defect filling, augmentation and reinforcement in combination with autogenous grafts. Among those, brushite cements ($CaHPO_4 \cdot 2H_2O$) showed good resorbability and solubility. If applied as a biphasic cement in combination with large granules of β-tricalcium phosphate (β-TCP; β-$Ca_3(PO_4)_2$) <0.5mm in diameter), they proved to be resorbed and replaced with new bone within 4-6 months in a drill hole model in long bone metaphyseal and epiphyseal application in sheep. Although, their biocompatibility was considered optimal at 2, 4 and 6 months, the immediate reaction of the tissue to the biphasic cement was unknown. In this study, the immediate reaction of a brushite biphasic liquid cement (ChronOs Inject) was studied.

METHODS: Eight (8) adult, Swiss Alpine sheep served as experimental animals and were divided in fours groups with 2 animals each. An osteotomy in the proximal tibia was performed, where a rectangular bone wedge of 0.7cm height was removed at the cranial aspect of the tibia plateau. The osteotomy extended ca.60% (2.4 cm) caudally into the tibia shaft and was made according to a standardized template. The defects were stabilized using a 3.5 mm T-plate and 7 x 3.5 mm screws and they were filled with the cements. The hind limbs were operated alternately and additional immobilization of the limbs was provided with splint bandages. A suspension system was used for 4 weeks to protect the animals from refracturing their limbs. The study period until sacrifice of animals was 2,4,6 and 8 weeks. After sacrifice, the bone samples were immediately harvested, macroscopically assessed and processed for histology. Non-decalcified bone specimens were embedded in acrylic resin (HistoDur®). Ground sections (30-40µm) and thin (5µm) were prepared, and stained with either toluidine blue or von Kossa/McNeal.

RESULTS: All cement samples were well integrated at the time of sacrifice, and were easily visible from outside of the bone. Histologic evaluation was performed focusing on cellular reactions and ways of cement degradation. Both cortices of the tibia defects were not remodeled yet at all time points. However, periosteal reactions and new bone formations had started at 6 weeks. A small resorption zone between the old bone matrix and the bulk of the cement was noticed (≈1-2 mm) mainly in the 2 weeks group. It gradually decreased over time. Resorption of the cement matrix (brushite) was quicker compared to the TCP granules. The gap within the resorption zone of the cement was filled with mesenchymal or osteoprogenitor cells and close to the old bone matrix active osteoblasts producing new osteoid were found at the bone surface already at 4 weeks. Small areas of new bone deposition were already noticed on the TCP granules in the 6 weeks group. Only in the 2 weeks group multinuclear foreign body cells were found. Macrophages digesting the cement particles were abundant after 4 weeks as well as actively osteoid synthesizing osteoblasts.

DISCUSSION & CONCLUSIONS: The biphasic resorbable brushite cement (ChronOs Inject) showed good biocompatibility also in short-term experiments. The immediate tissue reaction at short intervals revealed excellent tissue compatibility, such that no significant inflammatory reaction was present at 2,4, 6, and 8 weeks. Foreign body cells were seen only transiently at 2 weeks and were already completely replaced by cement digesting macrophages at 4 weeks. In any case, macrophages are normally involved in cellular debridement and are not considered to be inflammatory cells, at least in bone. The front of cement resorption and bone formation was parallel over time, although the resorption zone of the cement matrix was slightly larger initially at 2 weeks. In conclusion, the brushite cement as investigated in this study appears to be an excellent synthetic bone replacement also in short-term experiments.

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