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The effect of an octacalcium phosphate co-precipitated gelatin composite on the repair of critical-sized rat calvarial defects

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ABSTRACT

This study was designed to investigate the extent to which an octacalcium phosphate/gelatin (OCP/Gel) composite can repair rat calvarial critical-sized defects (CSD). OCP crystals were grown with various concentrations of gelatin molecules and the OCP/Gel composites were characterized by chemical analysis, X-ray diffraction (XRD), Fourier transform infrared (FTIR) spectroscopy, transmission electron microscopy (TEM), selected area electron diffraction (SAED) and mercury intrusion porosimetry. The OCP/Gel composite disks received vacuum dehydrothermal treatment, were implanted in Wistar rat calvarial CSD for 4, 8 and 16 weeks, and then subjected to radiologic, histologic, histomorphometric and histochemical assessment. The attachment of mouse bone marrow stromal ST-2 cells on the disks of the OCP/Gel composites was also examined after 1 day of incubation. OCP/Gel composites containing 24 wt.%, 31 wt.% and 40 wt.% of OCP and with approximate pore sizes of 10–500 μm were obtained. Plate-like crystals were observed closely associated with the Gel matrices. TEM, XRD, FTIR and SAED confirmed that the plate-like crystals were identical to those of the OCP phase, but contained a small amount of sphere-like amorphous material adjacent to the OCP crystals. The OCP (40 wt.%)/Gel composite repaired 71% of the CSD in conjunction with material degradation by osteoclastic cells, which reduced the percentage of the remaining implant to less than 3% within 16 weeks. Of the seeded ST-2 cells, 60–70% were able to migrate and attach to the OCP/Gel composites after 1 day of incubation, regardless of the OCP content. These results indicate that an OCP/Gel composite can repair rat calvarial CSD very efficiently and has favorable biodegradation characteristics. Therefore, it is hypothesized that host osteoblastic cells can easily migrate into an OCP/Gel composite.

1. Introduction

The capability to repair bone defects using alternative methods to the autograft is usually focused on the criteria needed to attain equivalent tissue engineering standards for healing large defects caused by trauma or disease in bone tissue [1]. Autologous bone is considered to be osteogenic [2], because it includes osteoblastic cells and growth factors, such as bone morphogenetic proteins (BMP), together with matrix materials, such as collagen and hydroxyapatite (HA) crystals, which are thought to work as osteoinductive and osteoconductive factors. A previous study reported that the implantation of autologous bone induced the regeneration of ~85% new bone in an experimentally created critical-sized defect (CSD) 15 mm in diameter in rabbit calvaria bone 16 weeks post-implantation [3]. A CSD is defined as a defect that does not heal spontaneously during the lifetime of the animal [4]. Another study demonstrated that the implantation of chitosan gels containing mesenchymal stem cells (MSC) and bone morphogenetic protein 2 (BMP-2) also induced the regeneration of over 80% of new bone in a CSD 8 mm in diameter in rat calvarial bone 8 weeks post-implantation [5]. Therefore, based on these studies using CSD models, an 80% regeneration rate of new bone could be considered the standard for achieving improvements in tissue engineering studies. However, it seems likely that the application of synthetic materials alone may not be as effective as introducing cells and/or growth factors, owing to the lack of osteogenic capability in most materials [6], although some reports have shown that synthetic calcium phosphate ceramics alone have osteogenic characteristics when used in large animal models, such as sheep [7,8]. Nevertheless, the use of synthetic materials alone without

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