Abstract

Effective reconstruction of large bone defects, particularly in thickness, remains as one of the major challenges in orthopedic and dental fields. We previously produced an E. coli-based industrial-scale GMP-grade recombinant human bone morphogenetic protein-2 (E-rhBMP-2) and showed that the combination of E-rhBMP-2 with beta-tricalcium phosphate (β-TCP/E-rhBMP-2) can effectively promote bone reconstruction. However, the limited mechanical strength and poor morphology retention of β-TCP granules are key points that need optimization to obtain more effective grafts and further expand its clinical applications. Therefore, we combined β-TCP/E-rhBMP-2 with fibrin gel to enhance its mechanical properties and usability for vertical bone regeneration. We investigated the mechanical properties and vertical bone regeneration effects of the materials, applied in conjunction with fibrin containing or not E-rhBMP-2 in a calvarial defect model in mice. Compression tests were conducted to assess the initial stability of the materials. Scanning electron microscope and Fourier transform infrared spectroscopy studies were conducted to characterize the presence of fibrin onto the scaffold. After 4 and 12 weeks of implantation, micro-computed tomography and histological and immunofluorescent analyses were performed to assess the morphology and volume of the newly formed bone. The fibrin-containing groups had significantly higher initial mechanical strength and higher ability to maintain its morphology *in vivo* compared to the counterparts without fibrin. However, fibrin gel alone suppressed the bone formation ability of β-TCP/E-rhBMP-2 whereas the presence of high doses of E-rhBMP-2 in fibrin gel resulted in material resorption and enhanced new bone formation. In conclusion, fibrin gel significantly improved the mechanical strength and surgical manageability of the β-TCP/E-rhBMP-2 scaffold, and the addition of E-rhBMP-2 to the fibrin gel further enhanced the vertical bone regeneration and initial structural integrity of the scaffold.

Keywords: BMP-2, Fibrin, Vertical Bone Regeneration, Biocompatible Materials.