Enhancement of posterolateral lumbar spine fusion using recombinant human bone morphogenetic protein-2 and mesenchymal stem cells delivered in fibrin glue.

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Abstract:

Mesenchymal stem cells have shown great potential for accelerating bone healing. In the present study, we evaluate the efficacy of fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 composite for posterolateral spinal fusion in a rabbit model. Forty adult rabbits underwent posterolateral intertransverse fusion at the L5-L6 level. The animals were randomly divided into four groups based on the implant material: fibrin glue, fibrin glue/mesenchymal stem cells composite, fibrin glue-recombinant human bone morphogenetic protein-2 (fibrin glue/recombinant human bone morphogenetic protein-2) composite, and fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 composite. After six weeks, the rabbits were euthanized for manual palpation, radiographic examination, biomechanical testing, and histology. Manual palpation results showed that the fusion rate for fibrin glue, fibrin glue/mesenchymal stem cells, fibrin glue/recombinant human bone morphogenetic protein-2, and fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 was 0, 0, 40%, and 70%, respectively. Moreover, fusion rate determined by radiographic examination for fibrin glue, fibrin glue/mesenchymal stem cells, fibrin glue/recombinant human bone morphogenetic protein-2, and fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 was 0, 0, 40%, and 80%, respectively. Gray analysis showed that fibrin glue/recombinant human bone morphogenetic protein-2 group had higher ossification area and density than fibrin glue group; and fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2

group had higher ossification area and density than fibrin glue/recombinant human bone morphogenetic protein-2 group. Formation of continuous bone masses between L5 and L6 level in mesenchymal stem cells/recombinant human bone morphogenetic protein-2/fibrin glue group was further confirmed by computed tomography scanning and three-dimensional reconstruction. Biomechanical testing demonstrated that the fusion strength (flexion, extension, lateral bending, and axial rotation) in fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 group is significantly higher than that in fibrin glue/recombinant human bone morphogenetic protein-2 group. The formation of mature bone tissues between transverse processes of the fused specimens from both fibrin glue/recombinant human bone morphogenetic protein-2, and fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 groups was confirmed by HE staining, and quantitative real-time polymerase chain reaction results showed the upregulation of CD31, type I collagen, osteocalcin, and osteonectin in the fibrin glue/mesenchymal stem cells/recombinant human bone morphogenetic protein-2 group. In conclusion, our findings show that mesenchymal stem cells delivered with recombinant human bone morphogenetic protein-2 using fibrin glue as carrier are more effective in enhancing spine fusion than recombinant human bone morphogenetic protein-2 without mesenchymal stem cells in the rabbit model.