ARTICULAR CARTILAGE REPAIR BY TRANSPLANTING VARIOUS CONCENTRATIONS OF HUMAN UMBILICAL CORD BLOOD-DERIVED MESENCHYMAL STEM CELLS AND HYALURONIC ACID HYDROGEL COMPOSITES IN A RABBIT MODEL

C.-W. Ha, J.-A. Kim, J. Rhim, J.-H. Shim, M.-J. Kim, W.-J. Han, S.-A. Heo, Y.-B. Park. Samsung Med. Ctr., Stem Cell & Regenerative Med. Res. Ctr., Sungkyunkwan Univ. Sch. of Med., Seoul, Republic of Korea

Purpose: Mesenchymal stem cells (MSCs) have shown therapeutic potential for cartilage repair in vitro and in vivo study. The investigations, however, on the optimal cell concentration of MSCs for the cartilage repair is still scarce. Therefore, we aimed to investigate the cartilage repair based on the transplantation of different concentrations of human umbilical cord blood derived mesenchymal stem cells (hUCB- MSCs) with 4 % hyaluronic acid (HA) hydrogel in a rabbit model. Methods: Critical-sized osteochondral defects, 3 mm wide 3 mm deep, were created in the center of the trochlear groove of femur. The left knee was used as an individual control by leaving the created defect untreated, and four experimental groups (11 rabbits/group) were given the composite (hUCB-MSCs and 4% HA) directly into the defect (0.2 ml/ cm^2) with various MSCs concentrations: 0.1, 0.5, 1.0, and 1.5 x 10^7 cells/ ml in each group. At 4, 8, and 16 weeks after transplantation, the degree of cartilage repair was evaluated grossly and histologically using a Carranze-Bencano scoring system.

Results: Transplanting hUCB-MSCs and a HA hydrogel composite resulted in overall superior cartilage repair tissue with better quality than no treatment. The defects in the experimental groups were gradually replaced by hyaline-like cartilage filling up to the height of the surrounding normal cartilage. The defect areas in the control group were filled with adipose and fibrotic cells. The experimental group showed stronger staining in Safranin-O staining, Masson's trichrome, and type II collagen immunostaining. The quantitative histologic evaluation of the cartilage revealed that the study groups were sig- nificantly superior to the control group with overall greater mean scores for histological evaluation. At 4 weeks post-transplantation, 0.5 x 10^7 cells/ml group showed highest score and then followed by 0.1 x 10^7 cells/ml group. At 8 weeks post-transplantation, 1.0 x 10^7 cells/ml group showed highest score and then 0.5 x 10^7 cells/ml group fol- lowed. At 16 weeks post-transplantation, 0.5 x 10^7 cells/ml group showed highest score and then 0.1 x 10^7 cells/ml group followed. High cell seeding density in hUCB-MSCs (1.510^7 cells/ml) was not favor- able for cartilage repair.

Conclusions: These findings suggest that transplantation of hUCB- MSCs and HA composites may be an effective candidate for the regenerative treatment of full thickness articular cartilage defects. As the results are variable according to the concentration of transplanted cells, the optimal cell density for MSCs transplantation for cartilage repair needs to be further investigated.

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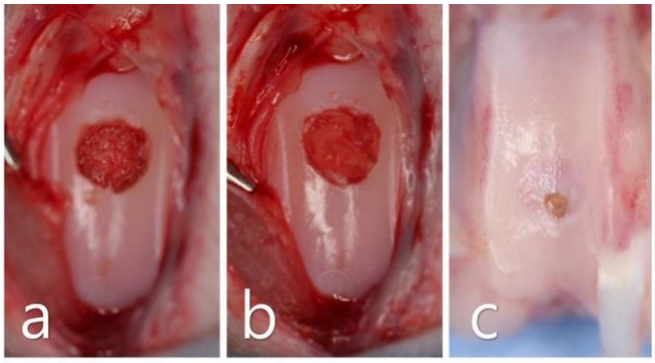

Figure 1. (a) Osteochondral defect was made on the trochlear groove, and PRP embedded HA/CS gel was applied (b). Cartilage was regenerated at the defect site, but the small crater was remained in central area (c).