

The Synergistic Effects of Mesenchymal Stem Cell Exosome and Hyaluronic Acid Combination Therapy on Cartilage Repair in a Rabbit Osteochondral Defect Model

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Aims: Osteochondral defects of the knee remain a significant source of morbidity worldwide. Cellular therapies involving mesenchymal stem cells (MSCs) are improving, and it is increasingly believed that their therapeutic efficacy lies in their tropism, with exosomes being a key modulator. The aim of this study was thus to compare the quality of cartilage regeneration with injectable MSC exosomes and hyaluronic acid (HA) combination therapy compared to HA alone in a rabbit osteochondral defect model. We hypothesised that the combination injection would result in superior cartilage regeneration compared to HA alone.

Methods: Seventeen rabbits were used in this study. Critical-sized osteochondral defects were surgically created in their trochlear grooves bilaterally. They were randomly allocated to receive three intra-articular injections with either HA alone (n=16) or a combination of HA and exosomes (n=18). The injections were administered immediately post-surgery, and on days seven and 14 post-surgery respectively. The rabbits were sacrificed at six and 12 weeks post-surgery. Cartilage assessment was performed by a blinded assessor using the ICRS repair assessment tool, and histomorphometric analysis with Wakitani and modified O'Driscoll scores. Functional competence of the repaired cartilage was assessed via biomechanical testing – focal axial compression stiffness of five different points of the regenerated cartilage was measured.

Results: There were significantly better overall ICRS scores at both 6 and 12 weeks in the combination therapy group. Wakitani and modified O'Driscoll histological scores for the combination therapy group were also significantly better at both 6 and 12 weeks. In addition, there was deterioration of the HA group scores over time. Biomechanically, the cartilage stiffness was significantly higher both centrally and peripherally in the combination therapy group at 6 and 12 weeks.

Conclusion: Three weekly injections of MSC exosomes and HA result in better quality functional cartilage regeneration compared to HA alone in a rabbit osteochondral defect model.