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Mesenchymal Stem Cell Exosomes Promote Growth Plate Repair and Reduce Limb Length Discrepancy in Young Rats - A Pilot Study

Tan SHS; Wong KL; Zhang S; Lim SK; Hui JH; Toh WS

Aims: The objective of this study was to examine the therapeutic effects of human mesenchymal stromal/stem cell (MSC) exosomes in an immunocompetent rat model of growth plate injury.

Methods: Exosomes were purified from conditioned medium of human MSCs by size-fractionation. Growth plate defect was surgically created on the right distal femur of 40 female Sprague-Dawley rats. Single intra-articular injection of 100 µg exosomes in 100 µL phosphate-buffered saline (PBS) or equivalent volume of PBS was given to the right knee immediately after the surgery. At 4 and 8 weeks post-treatment, limb length was measured by micro-computed tomography, and tissue repair was assessed by histology, immunohistochemistry and histomorphometric analyses.

Results: Single injection of MSC exosomes significantly increased limb length from 3.29 ± 0.07 cm at 4 weeks to 3.37 ± 0.11 cm at 8 weeks ($P = 0.047$) with no improvement in the vehicle control (PBS) group. The limb length discrepancy between the operated limb and the contralateral unoperated limb in exosome-treated group was significantly lesser than the discrepancy in PBS-treated group at both 4 weeks (2.52 ± 1.30% versus 4.11 ± 0.93%; $P = 0.006$) and 8 weeks (5.27 ± 2.11% versus 8.06 ± 2.56%; $P = 0.016$). Consistent with the reduced limb length discrepancy, the exosome-treated group displayed significantly higher percentage areal deposition of sulphated glycosaminoglycan ($P < 0.05$) and type II collagen ($P < 0.05$) than PBS-treated group at 8 weeks. However, bone bridge formation was not inhibited in both groups.

Conclusions: Single intra-articular injection of MSC exosomes significantly enhanced physeal repair and reduced limb length discrepancy but failed to inhibit bone bridge formation. This proof-of-concept pilot study demonstrates for the first time the potential use of MSC exosomes as a minimally invasive cell-free therapeutic in growth plate injuries to promote physeal repair and reduce limb length discrepancy.