

Effect of Locally Injected Mesenchymal Stem Cells on Bone Regeneration of Rat Calvaria Defects

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Abstract : Bone tissue presents great capacity to regenerate when injured by trauma, infectious processes, or neoplasia. However, the extent of injury may exceed the inherent tissue regeneration capability demanding some kind of additional intervention. In this scenario, cell therapy has emerged as a promising alternative to treat challenging bone defects. This study aimed at evaluating the effect of local injection of bone marrow-derived mesenchymal stem cells (BM-MSCs) and adipose tissue-derived mesenchymal stem cells (AT-MSCs) on bone regeneration of rat calvaria defects. BM-MSCs and AT-MSCs were isolated and characterized by expression of surface markers; cell viability was evaluated after injection through a 21G needle. Defects of 5 mm in diameter were created in calvaria and after two weeks a single injection of BM-MSCs, AT-MSCs or vehicle-PBS without cells (Control) was carried out. Cells were tracked by bioluminescence and at 4 weeks post-injection bone formation was evaluated by micro-computed tomography (μ CT) and histology, nanoindentation, and through gene expression of bone remodeling markers. The data were evaluated by one-way analysis of variance ($p \leq 0.05$). BM-MSCs and AT-MSCs presented characteristics of mesenchymal stem cells, kept viability after passing through a 21G needle and remained in the defects until day 14. In general, injection of both BM-MSCs and AT-MSCs resulted in higher bone formation compared to Control. Additionally, this bone tissue displayed elastic modulus and hardness similar to the pristine calvaria bone. The expression of all evaluated genes involved in bone formation was upregulated in bone tissue formed by BM-MSCs compared to AT-MSCs while genes involved in bone resorption were upregulated in AT-MSCs-formed bone. We show that cell therapy based on the local injection of BM-MSCs or AT-MSCs is effective in delivering viable cells that displayed local engraftment and induced a significant improvement in bone healing. Despite differences in the molecular cues observed between BM-MSCs and AT-MSCs, both cells were capable of forming bone tissue at comparable amounts and properties. These findings may drive cell therapy approaches toward the complete bone regeneration of challenging sites.

Keywords : cell therapy, mesenchymal stem cells, bone repair, cell culture

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