**The effects of staged intra-articular injection of cultured autologous mesenchymal stromal cells on the repair of damaged cartilage: a pilot study in caprine model**

ABSTRACT

INTRODUCTION: Treatment of chondral injuries remains a major issue despite the many advances made in cartilage repair techniques. Although it has been postulated that the use of marrow stimulation in combination with cell-based therapy may provide superior outcome, this has yet to be demonstrated. A pilot study was thus conducted to determine if bone marrow derived mesenchymal stromal cells (BM-MSCs) have modulatory effects on the repair outcomes of bone marrow stimulation (BMS) techniques. METHODS: Two full-thickness chondral 5 mm diameter defects were created in tandem on the medial condyle of left stifle joints of 18 Boer caprine (N = 18). Goats were then divided equally into three groups. Simultaneously, bone marrow aspirates were taken from the iliac crests from the goats in Group 1 and were sent for BM-MSC isolation and expansion in vitro. Six weeks later, BMS surgery, which involves subchondral drilling at the defect sites, was performed. After two weeks, the knees in Group 1 were given autologous intra-articular BM-MSCs (N = 6). In Group 2, although BMS was performed there were no supplementations provided. In Group 3, no intervention was administered. The caprines were sacrificed after six months. Repairs were evaluated using macroscopic assessment through the International Cartilage Repair Society (ICRS) scoring, histologic grading by O'Driscoll score, biochemical assays for glycosaminoglycans (GAGs) and gene expressions for aggrecan, collagen II and Sox9. RESULTS: Histological and immunohistochemical analyses demonstrated hyaline-like cartilage regeneration in the transplanted sites particularly in Group 1. In contrast, tissues in Groups 2 and 3 demonstrated mainly fibrocartilage. The highest ICRS and O'Driscoll scorings was also observed in Group 1, while the lowest score was seen in Group 3. Similarly, the total GAG/total protein as well as chondrogenic gene levels were expressed in the same order, that is highest in Group 1 while the lowest in Group three. Significant differences between these 3 groups were observed (P <0.05). CONCLUSIONS: This study suggests that supplementing intra-articular injections of BM-MSCs following BMS knee surgery provides superior cartilage repair outcomes.

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| **Keyword:** | Intra-articular injection; Mesenchymal stromal cells; Damaged cartilage; Caprine model; Bone marrow stimulation techniques |