Stem cells and basic fibroblast growth factor failed to improve tendon healing: an in vivo study using lentiviral gene transfer in a rat model.

Abstract:

The aim of this controlled study was to investigate the influence of mesenchymal stem cells (MSCs) and lentiviral (LV) expression of basic fibroblast growth factor (bFGF) on tendon remodeling in an in vivo rat model of an Achilles tendon defect. In eighty-four male Lewis rats, complete 2.4-mm tendon defects were created and were either left untreated (the phosphate-buffered saline solution [PBS] group) or were treated with mesenchymal stem cells expressing enhanced green fluorescent protein (the MSC-LV-eGFP group) or with mesenchymal stem cells expressing basic fibroblast growth factor lentivirally (the MSC-LV-bFGF group). After fourteen and twenty-eight days, the tendons were harvested and analyzed biomechanically and immunohistologically. After fourteen days, both mesenchymal stem cell groups were slightly superior in biomechanical testing. However, only the PBS control group showed a significant increase in biomechanical results over time (fourteen versus twenty-eight days; p = 0.012). Biomechanical results were better after twenty-eight days for the control group than for both MSC groups. However, the difference was significant only with regard to the stiffness results in the comparison of the PBS control and the eGFP stem cell group (p = 0.024). Histologically, the MSC groups had no better results than the control group.
after fourteen and twenty-eight days. In immunohistology, only labeling for type-I procollagen was strongly increased in both MSC groups in comparison with the PBS control group (p = 0.0009 for the MSC-LV-bFGF group and p = 0.0041 for the MSC-LV-eGFP group at fourteen days, and p = 0.004 and p = 0.132, respectively, at twenty-eight days). There were no significant differences in the immunohistological results between the stem cell groups. The biomechanical and immunohistological results showed that mesenchymal stem cells in both groups had only partially positive effects on tendon remodeling in the initial stages; however, in later stages, stem cells had potentially negative effects on biomechanical results. The additional expression of bFGF in stem cells had negligible effects on tendon remodeling. Preliminary studies using stem cells are partially promising; however, there are no relevant clinical data showing that stem cells are of significant benefit. The present study should lead to a more critical evaluation and thoughtful use of stem cells in humans until more clinical data are available.