Effects of Low-Intensity Pulsed Ultrasound, Dexamethasone/ TGF-β1, BMP-2 on the Transcriptional Expression of Human Mesenchymal Stem Cells: Chondrogenic vs. Osteogenic Differentiation

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Introduction

Mesenchymal stem cells (MSCs) are thought to have the greatest potential for differentiation into chondrocytes and osteocytes (1). Moreover, chondrogenic differentiation of animal MSCs was reportedly enhanced by the application of LIPUS in 3 D models (2). We aim to investigate the effects of low-intensity pulsed ultrasound (LIPUS) on chondrogenic vs. osteogenic differentiation in hMSCs.

Materials and Methods

Human MSCs (hMSCs) were subjected to LIPUS with and without dexamethasone/transforming growth factor -β1 (TD) or bone morphogenetic protein-2 (BMP-2). A real-time polymerase chain reaction (PCR) was used to assess the effects on messenger RNA (mRNA) expression of several genes associated with chondrogenesis and osteogenesis.

The continuous variables were presented as mean and standard deviation, and one-way ANOVA was used to compare the means of the continuous variables between groups at once.

Results

TD-treated hMSCs showed significant chondrogenic morphology and increase in mRNA expression of chondrogenic markers such as Sox-9, aggrecan, and type II collagen at weeks 2 and 3. Co-treatment with LIPUS and TD revealed a synergistic effect of chondrogenic markers on mRNA expression at weeks 2 and 3. Runx2, an osteogenic transcription factor, showed no effect on TD treated groups either with or without LIPUS; however, a significant increase in the mRNA expression of Runx2 was found only in the LIPUS group at week 1. A morphological shift from an elongated fibroblast-like cell type to a shorter appearance was detected 3 days after LIPUS and/or BMP-2 treatment. Increases in the mRNA expressions of osteogenic markers such as Runx2 and ALP were also observed. Combined treatment of LIPUS and BMP-2 showed no synergistic effect.

Discussion and Conclusions

The present study attempts to characterize the effects of LIPUS alone and in combination with cytokines TD and BMP-2 on both chondrogenic and osteogenic differentiation. LIPUS enhances TD-mediated transcriptional expression of chondrogenic differentiation of hMSCs. LIPUS alone can increase transcriptional expression of osteogenic differentiation of hMSCs. LIPUS may act in a different manner clinically on bone versus cartilage repair.

References

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Acknowledgments

NSC94-2320-B-038-013

Disclosures

All authors have nothing to disclose.