

Shock Wave Therapy as an Alternative to Cardiac Cell Therapy – An In-Vitro Examination

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Device and producing company:

DermaGold CP-155 (Tissue Regeneration Technologies, LLC, Woodstock, USA manufactured by MTS Europe GmbH, Konstanz, Germany)

Introduction:

Recently it has been well documented that shock waves at low energy levels induce tissue regenerative effects. Transthoracic application of shock waves (SW) can be shown to augment myocardial vascularization in a porcine model of myocardial infarction. SW even improve myocardial perfusion and cause relief of angina symptoms in human patients with severe coronary artery disease. Nevertheless the underlying mechanism remains largely unknown.

Methods:

Primary cell cultures of endothelial cells and fibroblasts were established from native rat hearts. Additionally H9C2-cardiomyocytes (American Type Culture Collection) were used. A thermostatically controlled water bath was designed to avoid distracting physical effects. Adherent cells in common cell culture flasks filled with culture medium were dunked into the water bath. Unfocused SW at an energy flux density of 0.15 mJ/mm² were applied to the cells with a frequency of 5 Hz. Non-treated cells were used as a control group. Number of cells and their vitality were analysed over a period of 7 days. Numerous analyses of immunohistochemistry and molecular biology were performed.

Results:

SW stimulate every cardiac cell type to a different extent. Each cell type reacts at a different time point after treatment as well. The distance between the applicator and the cells and the energy flux density have a strong influence on the cells' behaviour. Between day 4 and day 5 the duplication time of treated cells was significantly higher compared to controls. Immunohistochemistry and molecular biology show significant differences in the gene expression of MMP's, TIMP's and collagen. Treated cells also alter their cytoskeleton (Vimentin, Tubulin, beta-Actin) and show significantly more proliferation (Ki-67) and changes in the expression of adhesion molecules (CD31) as well as connexins 40, 43, 45. No apoptosis was found in the treatment group.

Discussion:

SW activate proliferation of cardiac cells. Endothelial cells proliferate fastest, which underlines the known effect of neovascularization in-vivo. Moreover, cells alter the assembly of microfilaments, and thus seem to ameliorate cell migration. Changes in the MMP and TIMP levels, as well as the expression of adhesion molecules seem to be strongly involved in the SW tissue regenerative effect on ischemic myocardium.