

Pulsed Acoustic Cellular Therapy Supports Pro-angiogenic Factors Expression in Ischemic Muscles

Purpose: Tissue ischemia alters tissues circulations and affects wound healing. Pulsed Acoustic Cellular Therapy (PACE) tested neovascularization of ischemic muscles.

Methods: Cremaster muscles intravital microcirculation recorded: 1) Non-ischemic controls, 2) 5hrs ischemia control; 3) pre-ischemic (5hrs) PACE therapy 4) post-ischemic (5hrs) PACE therapy.

Assessments: Microcirculatory hemodynamics (capillary perfusion, leukocyte-endothelial interactions); immunohistochemistry (leukocyte trafficking - cell adhesion molecules: E-selectin, ICAM-1 and VCAM-1; vasculogenesis: VEGF, von Willebrand factor (vWF).

Taqman real-time RT PCR gene expression: pro-angiogenic factors (Vegfa, Vwf, eNos) and, pro-inflammatory factor (iNos) and pro-angiogenic chemokines: CCL2, CXCL5.

Results: Pre-ischemic PACE therapy decreased rolling and sticking leukocytes and this correlated with down-regulation of ELAM-1 and ICAM-1 and lack of VCAM-1 expression compared to ischemic controls. Post-ischemic PACE increased functional capillary density, decreased activation of rolling and sticking leukocytes that correlated with down-regulation of ELAM-1 and VCAM-1. Post-ischemic PACE resulted in up-regulation of VEGF and vWF expression on the vessel endothelium.

Pre-ischemic treatment favored expression of pro-angiogenic gene Vegf, inflammatory gene iNos and CXCL5, CCL2 chemokine but had no effect on Vwf and eNos gene expression. Post-ischemic treatment decreased gene expression of pro-inflammatory factor (iNos).

Conclusions:

Pre-ischemic and post-ischemic PACE down-regulated adhesion molecules expression and this correlated with reduction of sticking leukocytes in microcirculation. Post-ischemic PACE therapy inhibited inflammatory responses by reduced expression of pro-inflammatory genes, had no negative impact on expression of pro-angiogenic genes and induced expression of pro-angiogenic factors (VEGF, vWF) which correlated with increased neoangiogenesis.