ADMINISTRATION OF HEMATOPOIETIC PROGENITOR CELLS IMPROVED LIMB PERFUSION AND NEOVASCULGENESIS VIA UPREGULATION OF THE ANG-2/TIE-2 PATHWAY

Moderated Poster Contributions
Poster Sessions, Expo North
Sunday, March 10, 2013, 3:45 p.m.-4:30 p.m.

Session Title: Cell Therapy and Angiogenesis
Abstract Category: 42. TCT@ACC-i2: Cell Therapy & Angiogenesis
Presentation Number: 2110M-227

Authors: Georgia Vogiatzi, Dimitris Tousoulis, Alexandros Briasoulis, Aggeliki Valatsou, Anna-Maria Kampoli, Charalambos Antoniades, Christina Chrysochoou, Kostas Toutouzas, Costas Tentolouris, Despoina Perrea, Christodoulos Stefanadis, 1st Cardiology Unit, Athens University Medical School, Athens, Greece

Background: Bone marrow derived progenitor cells have been suggested to promote postnatal neovascularization. In this study we investigated whether direct intramuscular infusion of enriched hematopoietic cells, improved limb perfusion in a murine model of hind limb ischemia.

Methods: Wild type C57BL/6 male mice underwent unilateral hind-limb ischemia, were divided in three groups (n=12/group) and received a single intramuscular injection of 1x10^6 Lin-/sca+ cells, or granulocyte colony-stimulating factor (G-CSF) for 7 days or normal saline. Each group mice underwent Laser Doppler perfusion Imaging on days 1, 7 and 28 after surgery for the estimation of the bilateral hind-limb perfusion. At day 28 they were sacrificed and quantitative real time RT-PCR was performed to the muscle tissues from both limbs to analyze the differential gene expression of vascular endothelial growth factor (VEGF), Tie-2, Ang-1 and Ang-2. Muscle tissue sections were stained with rat anti-CD31 antibody. Capillaries and arterioles in the ischemic areas were counted with confocal microscopy at day 28.

Results: Ischemic/non ischemic ratio was significantly increased in ischemic limbs of cell- and G-CSF-treated mice versus control mice at 7 days (p<0.05 vs control), which was maintained at 28 days (p<0.05 vs control) only in the cell-treated group. There was no significant increase of ischemic/nonischemic ratio in the cell-treated mice compared with G-CSF at day 7 or day 28 (p=NS). Capillary density was increased in the cell-treated group compared to G-CSF-treated group and control (p<0.05). No difference in the capillary density between the G-CSF-treated and the control group was observed. Compared to the G-CSF and control group, the expression of VEGF (p<0.05), Ang-2 (p<0.05) and sTie-2 (p<0.05) were significantly increased in the ischemic limbs of the Epo-treated group. In contrast, the Ang-1 expression didn’t significantly differ between the three groups.

Conclusion: Direct intramuscular infusion of lin-/sca+ significantly improves blood flow and increases neoangiogenesis by upregulation of the Ang-2/Tie-2 pathway when compared with G-CSF and control treatment in ischemic limbs.