Biodegradable Scaffolds Incorporating Vascular Endothelial Growth Factor as a Novel Sustained Delivery Platform to Induce Angiogenesis

Qinghua Sun, Ruth Chen, David J. Mooney, Sanjay Rajagopalan, P. Michael Grossman, University of Michigan Hospitals and Health System, Ann Arbor, MI

Background: Therapeutic angiogenesis strategies have focused on protracted delivery of growth factors using gene transfer approaches that are limited by potential toxicity and diminished transfection rates. Polymer formulations can deliver drugs locally over time. We hypothesized that protracted delivery of vascular endothelial growth factor (VEGF) using a polymer (85:15 poly lactide-co-glycolide (PLG)) would result in stable neovascular networks.

Methods: C57BL/6 mice (n = 5/group) underwent unilateral hindlimb ischemia surgery and were randomized to surgery only (No PLG), surgery followed by implantation of scaffolds incorporating 3µg of VEGF165 (PLG-VEGF). At various time points, blood flow was assessed using Laser Doppler perfusion index (LDPI, ischemic/nonischemic limb %), local tissue VEGF content was measured by ELISA, and tissues were immunostained with CD31 and α-smooth muscle actin (α-SMA).

Results: The PLG-VEGF formulation resulted in protracted release of VEGF (384 ± 34 pg/ml at week 4). PLG-VEGF was associated with significantly better perfusion and enhanced CD31 and α-SMA immunostaining (Table).

Conclusion: PLG-VEGF scaffolds results in sustained VEGF delivery, improved tissue perfusion, greater capillary density, and more mature vasculature compared to controls. The control-released PLG polymer system is a promising delivery system for therapeutic neovascularization applications.

Effects of Growth Hormone on Circulating Cytokine Dysbalance and Left Ventricular Geometry in Patients With Idiopathic Dilated Cardiomyopathy

Stamatis Adanapoulos, John T. Parissis, Dimitrios Karatzas, John Paraskevaidis, George Karavolias, Dimitrios Degianiannis, Dimitrios Kremastinos, Onassis Cardiac Surgery Center, Athens, Greece

Background: Experimental studies have demonstrated that growth hormone (GH) can influence left ventricular (LV) myocardial growth and remodeling in the setting of chronic heart failure (CHF). This study investigates whether the effects of GH on LV geometry are associated with the respective modulation of circulating proinflammatory/anti-inflammatory cytokine balance in patients with CHF secondary to idiopathic dilated cardiomyopathy (IDC).

Methods: Plasma proinflammatory cytokines TNF-α, IL-6, MCP-1 and anti-inflammatory molecules IL-10 and TGF-β2 were measured (ELISA) in 12 IDC patients (NYHA class III; LVEF < 40%). A good correlation was found between GH-induced reverse LV remodeling expressed by the percentage reduction in LV end-systolic volume index (LVESVI; p = 0.005) and the increase in plasma IL-10/TNF-α ratio (r = 0.53, p < 0.01). VO2max (15.3 ± 0.7 vs 17.1 ± 0.9 ml/kg/min, p < 0.05) was also found in LVESVI and VO2max (3.1 ± 0.6 vs 4.4 ± 0.6, p < 0.05) were observed in IDC patients after GH treatment. A significant reduction in LV end-systolic volume index (LVESVI, 128 ± 12 vs 102 ± 12 ml/m2, p < 0.01) and LV end-diastolic volume index (LVEDVI, 228 ± 16 vs 200 ± 14 ml/m2, p < 0.05), as well as a significant increase in posterior wall thickness (PWT, 9.2 ± 0.5 vs 10.3 ± 0.6 mm, p < 0.001) and VO2max (15.3 ± 0.7 vs 17.1 ± 0.9 ml/kg/min, p < 0.05) were also found. A good correlation was found between GH-induced reverse LV remodeling expressed by the percentage reduction of LVESVI and percentage increase in exercise tolerance expressed by VO2max (r = -0.53, p < 0.05). Finally, GH-induced reduction in LVESVI was significantly correlated with respective increase of plasma IL-10/TNF-α ratio (r = 0.62, p < 0.01).

Conclusions: GH administration modulates beneficially circulating cytokine balance and causes reverse LV remodeling in patients with CHF and IDC. Immunoregulatory effects of GH may be associated with the improvement of exercise capacity and LV geometry of IDC patients.