Promotion of Collateral Growth (Arteriogenesis) by Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) in Patients With Coronary Artery Disease

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Experimentally, activated macrophages have been documented to induce vascular proliferation. Methods: In 21 patients (pts; 11 men, age 74±7 years) with three-vessel coronary artery disease eligible for PTCA of ≥1 stenotic lesion, the effect of GM-CSF on quantitatively assessed collateral flow was tested in a randomized, double-blind, placebo-controlled fashion. The study protocol consisted of an invasive baseline and follow-up collateral flow index (CFI, no unit) measurement immediately before intracoronary (IC) injection of 40 μg of GM-CSF (n=10) or placebo (n=11), and after a 2-week treatment period with subcutaneous GM-CSF (10 μg/kg) or placebo, respectively. CFI was determined by simultaneous measurements of mean aortic (Pao2, mmHg), coronary wedge (Pcw, mmHg), and central venous pressure (CVP, mmHg): CFI=(Pao2-CVP)/(Pcw-CVP).

Results: CFI after before treatment 0.32±0.24 control and 0.21±0.14 GM-CSF.

Delta CFI after-before treatment +0.11 0.01 NS

Conclusion: CFI improved by GM-CSF sustaining during long-term follow-up, and whether alternative routes of administration are more effective.

Therapeutic Angiogenesis via Selective Retroinfusion of FGF-2 and VEGF Into the Femoral Vein in the Chronic Ischemic Hindlimb

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With the aim to enhance therapeutic angiogenesis by increasing tissue binding of angiogenic growth factors, selective retroinfusion of the femoral vein was performed in the chronically ischemic rabbit hindlimb. In separate scintigraphic experiments, tissue concentration of bFGF (500 pg) and VEGF Protein (20 pg) or saline [controls]. Results: There were fewer ischemic segments (a decrease in ischemic burden) after treatment in 50% (4/8) of the AIV pigs, versus 17% (1/6) of the IC pigs, and 0% (0/3) of the control pigs. The percentage of ischemic myocardial segments decreased by an average of 4% per pig in the IC arm, compared to an increase of 23% in the IC arm and 28% in the control arm (p<0.001, AIV compared to IC or control). Average flow (ml/min/gm tissue) in the AIV region during pacing increased significantly from pre-treatment to after treatment in the AIV arm by 22% (0.73 to 0.93, p=0.001). There was no echocardiographic evidence of ischemia in the IC arm (1.1 to 1.0, p=0.6), and decreased significantly by 20% in the control arm (1.4 to 1.1, p<0.04). Conclusion: Delivery of FGF-2 protein via ngn retrograde pressure, retrograde injection into the AIV may represent a practical and effective means for improving chronic myocardial ischemia.

High Pressure, Retrograde, Coronary Venous Delivery of FGF-2 Protein Improves Coronary Blood Flow In a Porcine Model of Myocardial Ischemia


Background: Effective delivery of angiogenic factors to ischemic myocardium remains a practical challenge. We compared delivery of FGF-2 protein via high pressure, retrograde injection into the anterior interventricular vein (AIV) with intracoronary (IC) administration in a porcine model of chronic myocardial ischemia. At 4 weeks, myocardial blood flow at rest and during pacing was measured in all pigs using fluoroscopic microspheres. In 8 pigs, FGF-2 protein (6 mcg/ml) was delivered via retrograde injection into the AIV at a pressure of 100 mmHg. Six pigs received a similar total amount of FGF-2 by IC delivery into the three major coronary arteries, and 3 pigs served as controls. Four weeks later, myocardial blood flow was reassessed. Post sacrifice, the hearts were divided into 48 segments, and myocardial flow in each segment was analyzed by microsphere evidence of ischemia prior to and 4 weeks after treatment. Ischemia was defined as a greater than 10% decrease in blood flow during pacing. The average absolute flow, during pacing, in the LAD region before and after treatment was also calculated for each arm.

Conclusion: CFI after before treatment 0.32±0.24 control and 0.21±0.14 GM-CSF.

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Conclusion: CFI improved by GM-CSF sustaining during long-term follow-up, and whether alternative routes of administration are more effective.