in rats transfected with the HGF gene compared with control vector at 4 weeks after transfection.

Conclusion: Overall, these results may indicate that the effect of angiogenesis by locally transfected HGF gene is not at least through the NO. Furthermore, transfected HGF gene may have the effect of angiogenesis in the several conditions of impaired NO synthesis.

1178-144
In Vivo Electroporation of Hepatocyte Growth Factor Gene Into Skeletal Muscle of a Cardiomyopathic Hamster Ameliorates Cardiac Dysfunction and Fibrosis

Yuko Tsujiita, Kazuo Komamura, Masafumi Kitakaze, Kunio Miyatake, National Cardiovascular Center, Osaka, Japan

Background: Hepatocyte growth factor (HGF) has potent angiogenic and anti-fibrotic effects. We examined whether the electroporation of HGF gene into skeletal muscle of dilated cardiomyopathy hamster could affect on cardiac function and fibrosis.

Methods: Plates with electroporation vector expressing HGF (920 ng) was transfected into the bilateral tibialis anterior muscles of 12 TO-2 hamsters of 11 weeks of age by electroporation once a week up to 14 weeks of age. Empty plates was transfected into other 19 hamsters. Echocardiographic, hemodynamic, histopathological and biochemical changes were measured before and after electroporation. Results: Electroporation increased the serum HGF levels to >10 ng/ml, in treated hamsters, whereas control hamsters showed no increase. LV ejection fraction (47.9±9.4 vs. 28.8±11.2 %, p<0.01), and E/A ratio (1.24±0.33 vs. 3.99±1.01, p<0.05) were better in treated hamsters than in control hamsters. Systemic vascular resistance (3.31±1.30 vs. 7.34±4.96 mmHg/ml/min) was lower in treated hamsters than in control hamsters. Although left ventricular weight to diastolic length ratio (12.6±1.2 vs. 12.9±1.2 mg/g, NS) was similar, area of fibrosis in the ventricles (11.8±3.4 vs. 17.8±3.5 %, p<0.05) and hydroxyproline content (3.7±0.7 vs. 5.1±0.9 mg/g, p<0.05) was less in treated hamsters than in control hamsters. Conclusions: These findings suggest that HGF gene transfer into muscle by electroporation is an effective means of delivery of HGF for treatment of heart failure due to dilated cardiomyopathy.

1178-145
Transfection With DNA of Soluble VCAM-1 Causes Monocyte Chemotaxis and Increased Endothelial Cell Staining: A New Gene-Therapeutic Approach for Angiogenesis

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Background: Monocytes have been described as local mediators of angiogenesis. For monocyte recruitment, chemotaxis and adhesion to endothelial cells are major prerequisites. We hypothesized that soluble parts of endothelial adhesion molecules act as chemotactic factors and thereby may promote angiogenesis.

Methods and Results: Soluble (s) Adhesion molecules were tested for chemotactic activity using the monocyte cell line U937 in a 46-well microchemotaxis chamber. Only sVCAM-1, but not sICAM-1 or sE-selectin exhibited a significant concentration-dependent chemotactic effect at concentrations between 10 to 675 nM. To test for a potential angiogenic effect of sVCAM-1, we designed an expression vector of a truncated form of the VCAM-1 gene encoding for sVCAM-1. After thorough cytotoxicity tests, rats were injected intramyocardially with naked sVCAM-1-DNA into the left ventricle. 21 days later, hearts were stained for macrophages with an ED1 antibody and for endothelial cells with indoxyl-tetrazolium (IT). Injection of sVCAM-1 DNA (n=10) results in 3.7±1.1 % of ED1 positive area (area without injection (control, n=10): 0.03±0.02 %, p<0.001) and in 5.5±2.2 % of IT positive area (control: 5.1±0.9 %, p<0.001). Injection controls with PBS (n=10), and the I9ial gene (n=10) did not reveal statistically significant differences in macrophage and endothelial cell staining.

Conclusions: Transfection of soluble-VCAM-1-DNA induces chemotaxis on monocytes and causes an increase in endothelial cell staining in rat hearts. Further studies are warranted to prove that the transfection of soluble-VCAM-1-DNA represents a potential gene therapeutic approach for angiogenesis.

POSTER SESSION

1179 Vascular Mechanics

Tuesday, April 01, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

1179-148
Is a Radial-Aortic Transfer Function for Total Arterial Compliance Robust in Women and the Elderly?

Hannah A. Cookson, Leanne Nott, Philip Pommar, Stephanie C. Carter, Thomas H. Marwick, University of Queensland, Brisbane, Australia, OLV Hospitaal, Aalst, Belgium

Background: Estimates of central aortic pulse pressure for total arterial compliance (TAC) are based on a radial-aortic transfer function to calculate central pressure from radial applanation tonometry. However, this approach has been validated in groups with a preponderance of middle-aged men, and its validity in women and older patients has been questioned.

Methods: Carotid and radial applanation tonometry were performed simultaneously with pulsed wave Doppler of the LVOT using specialised software, in 96 pts (47 men; age 56±8 y) with and without cardiovascular disease. TAC was calculated by the pulse-pressure method. Mean aortic pulse pressure (MAPP) was derived using a transfer function from radial tonometry, and then compared with the carotid waveform.

Results: The correlation between direct carotid measurement and radial measurement with the transfer function was good for TAC (r=0.91). However, there was a significant difference in TAC in older patients (>65 y) using the two waveform. Bland-Altman analysis of the difference (DIFF) between radial and carotid TAC showed significant differences between men and women (p<0.000) and between younger and older patients (p<0.05).

1179-147
Mental Stress Inhibits the Intimal Fibromuscular Proliferation Through Endogenous Opoid System in the Process of Arterial Remodeling

Kunimitsu Iwai, Masayuki Matsumoto, Kenichi Kawanishi, Yukihito Nishinuma, Hiroshi Murata, Ming Y. Tong, Toshiyuki Nakatani, Hideyuki Hattori, Shigeto Morimoto, Kanazawa Medical University, Ishikawa-ken, Japan

Purpose: Mental stress is speculated to be the trigger for the rupture of fibrous cap around the coronary atherosclerotic plaque. We investigated the influence of mental stress on the intimal fibromuscular proliferation in the rat model of arterial remodeling after endothelial injury in connection with two stress hormone systems. Methods and Results: In Wistar-Kyoto rats (eight groups,each n=10) the endothelium of abdominal aorta was denuded with balloon catheter. (1)denudation (2)denudation + immobilization(6hrs/d) (3)denudation + naltrexone (NAL)2mg/kg ip (4)denudation + NAL + immobilization (5)denudation + beta-endorphin(END:10ng/kg) (6)denudation + NAL + END (7) denudation + naltrexone+beta-endorphin+immobilization. The severity of intimal hyperplasia was highest in control group and NAL reduced this hyperplasia. The area ratio of intima to media (A/I) was significantly reduced by immobilization (p=0.05) and also was also reduced by NAL (p<0.05). Immunohistochemical studies on 3 days after denudation showed the parallel results with the noradrenaline formation. The migrating activity for the serum of media smooth muscle cells (SMC) assessed by PCNA immunohistochemically 3 days after denudation showed the parallel results with the noradrenaline formation. The migrating activity for the serum of media smooth muscle cells (SMC) assessed by PCNA immunohistochemically 3 days after denudation showed the parallel results with the noradrenaline formation. The migrating activity for the serum of media smooth muscle cells (SMC) assessed by PCNA immunohistochemically 3 days after denudation showed the parallel results with the noradrenaline formation. The migrating activity for the serum of media smooth muscle cells (SMC) assessed by PCNA immunohistochemically 3 days after denudation showed the parallel results with the noradrenaline formation.
Cardiac contractility was estimated by the cardiac power index (CPI). Cardiac index (CI), and pulmonary capillary wedge pressure have previously demonstrated abnormalities in the extracellular matrix turnover might involve the progressive elastic and hemodynamic worsening of patients with DCM.

Conclusions: These results suggest that 5-HT is involved in hindlimb ischemia in atherosclerotic lesions.

Methods: LDL induction in ApoE-/- mice caused a severe perilimus deficit in the ischemic leg with no neovascularization after 14 days in the vehicle group and 100% of foot necrosis by day 14. In contrast, incidence of foot necrosis was reduced by SEL65.0472 treatment (-66%, p<0.05) and was accompanied by an improved pedal perfusion ratio between the ischemic and the contralateral normal perfused limb. RT-PCR analysis revealed that both 5-HT1B and 5-HT2A receptors were expressed in aorta from ApoE-/- mice. However neither 3 nor 8 months of treatment with SEL65.0472 affected the development of atherosclerotic lesions.

Conclusions: These results suggest that 5-HT is involved in hindlimb ischemia in atherosclerotic lesions.