1211 Endogenous Factors Contributing to Ischemic Injury

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1211-131 Expression of Plasma Soluble Fas, an Apoptosis Inhibitor, and Plasma Soluble Fas Ligand, an Inducer of Apoptosis, in Patients With Acute Myocardial Infarction

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Background: It has been reported that apoptotic myocytes are seen in acute myocardial infarction (AMI). The Fas receptor (Fas) - Fas ligand (Fas-L) system is representative system of apoptosis. Fas on the cell membrane induces apoptosis when it binds Fas-L or soluble Fas ligand (sFas-L) expressed mainly from activated T cell. However, soluble Fas (sFas) blocks apoptosis by inhibiting their bindings on the cell membrane. We previously reported that plasma sFas, but not plasma sFas-L levels, in patients with chronic heart failure (CHF) were increased with the severity of CHF. However, plasma levels of sFas-L and sFas in patients with AMI are unknown.

Methods: In 22 patients (average age: 63 ± 2 yrs, mean ± SEM) with initial AMI (proximal LAD infarction, TIMI 0 or I, reperfused by direct PTCA within 6 hrs), 62 age- and gender-matched normal subjects, and 8 patients performed elective PTCA to stable angina, plasma sFas and sFas-L were serially assessed by sandwich ELISA using monoclonal anti-human antibodies.

Results: Plasma sFas level was not increased 3 or 6 hrs after the onset of AMI (sFas (ng/mL): 3 hrs: 1.73 ± 0.14, 6 hrs: 2.19 ± 0.32), but was significantly elevated 24 hrs (3.47 ± 0.17*, *p < 0.05 vs. Normal: 2.10 ± 0.12). Then, the level decreased 48 hrs (2.40 ± 0.22), and normalized at 240 hrs (2.07 ± 0.29).

However, plasma sFas-L was within the normal range in all samples during AMI. Plasma sFas levels 24 hrs after the onset of AMI correlated well with peak CPK levels (r = 0.75, p < 0.05) and infarcted size of AMI.

Conclusion: We found that plasma sFas level was increased in AMI, and correlated well with infarcted size of AMI. It may play an important role in the pathophysiology of AMI.

1211-132 Pacing-induced Ischemia Results in Transcardiac Activation of Leukocyte to Produce Tumor Necrosis Factor-α in Patients With Angina Pectoris

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Background: Transcardiac leukocyte activation during a brief myocardial ischemia has not been clarified.

Methods: We examined the effects of myocardial ischemia on cytokine production by lipopolysaccharide (LPS)-stimulated whole blood in patients with stable angina. The transcardiac activation of leukocyte to produce cytokines before and during rapid atrial pacing was assessed in 10 patients with stable exertional angina and the left anterior descending coronary artery disease (Group A) and in 10 control patients with chest pain but normal coronary artery (Group B). Heparinized blood was collected in the great cardiac vein (GCV) and aortic root simultaneously, diluted in RPMI, stimulated with LPS, and incubated for 24 hours. Tumor necrosis factor-α (TNF-α), interleukin (IL)-1 β, and IL-6 were measured by an enzyme-linked immunosorbent assay.

Results: The GCV-arterial differences of TNF-α increased significantly during pacing-induced ischemia in Group A (10 ± 260 to 115 ± 113 pg/ml, p < 0.01)(mean ± SD), but remained unchanged in Group B (15 ± 85 to −20 ± 90 pg/ml) in comparison with those before pacing. There were no such significant changes in GCV-arterial differences of IL-1 β (Group A: −52 ± 215 to −45 ± 139, Group B: −84 ± 210 to 88 ± 160 pg/ml) and IL-6 (Group A: −270 ± 1210 to 197 ± 280, Group B: 60 ± 320 to −220 ± 920 pg/ml).

Conclusion: These results suggest that a brief myocardial ischemia activates the potential of leukocytes to produce tumor necrosis factor-α in patients with ischemic heart disease.

1211-133 The Association Between a Polymorphism of the Endothelial Nitric Oxide Synthase Gene and the Risk of Acute Myocardial Infarction in the Young Population

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Smoking is the most prominent risk factor for acute myocardial infarction (AMI) in young patients. Genetic predisposition might also be important in the development of AMI in this group. Endothelium-derived nitric oxide (NO) has been shown to be involved in the smoking effects on the endothelium. We investigated the distribution of the endothelial nitric oxide synthase (*ecNOS*) gene a/b polymorphism in 72 AMI patients and 153 control subjects in relation to smoking status and age. The aa, ab, and bb genotypes were found in 5, 17, and 50 cases among AMI patients and 0, 34, and 119 cases among the control subjects. There was a significant correlation between the ecNOS polymorphism and AMI (p = 0.00487). The presence of the ecNOSa allele was also significantly related to the development of AMI (p = 0.038). When the correlation was analyzed by age, the significance only remained in the group below age 50 (p = 0.013). Smoking status and the ecNOS polymorphism had a synergistic effect in the risk of AMI. Young persons who are smoking and have the ecNOSa allele, especially aa homozygotes, may have an increased risk of developing AMI.

1211-134 Hemodynamic and Inotropic Effects of Endothelin Antagonists

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The potent vasoconstrictor endothelin-1 (ET-1) is involved in the development of several diseases and therapy with endothelin receptor antagonists may be of importance in future. Previous in vivo studies with a selective endothelin$_B$ (ET_B) receptor antagonist showed that the positive inotropy of ET-1 is mainly mediated by ET_B receptors while its vasoconstrictive effect is mainly mediated by endothelin$_A$ (ET_A) receptors. This study examined the effects of selective ET_A and ET_B receptor blockade on hemodynamics and myocardial contractility.

In open-chest rats the i.v. effects of the ET_A antagonist BQ 610 (0.15 μmol/kg) and the ET_B antagonist BQ 788 (0.5 μmol/kg) were compared with NaCl-controls. Additionally to measurements in the intact circulation isovolumic measurements (isovol. LVSP, isovol. dp/dt_{max}) were performed to determine myocardial contractility.

	CO	TPR	isovol. LVSP	isovol. dp/dt_{max}
BQ 610	126 ± 3†	86 ± 2*	100 ± 1*	106 ± 2*
BQ 788	117 ± 4	89 ± 3	94 ± 2	94 ± 2*
NaCl	111 ± 1	94 ± 1	96 ± 1	100 ± 1

Means ± SEM in % of preinfusion values * p < 0.05, † p < 0.01

While selective ET_A receptor blockade by BQ 610 causes vasodilatation with a consecutive increase of the cardiac output selective ET_B blockade with BQ 788 has no favourable effects on hemodynamics. The isovolumic measurements indicate a positive inotropic effect of BQ 610 and a cardiodepressive effect of BQ 788.

Conclusions: Selective ET_A blockade can unmask the positive inotropic effect of endogenous ET-1 via ET_B receptors. Thus ET_A blockade may be an advantage over unselective ET_A/ET_B blockade.

1212 New Discoveries in Unstable Angina

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1212-125 Coronary Stenting Versus Balloon Angioplasty for Unstable Angina

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While unstable angina (UA) has been associated with increased complications and restenosis after conventional balloon angioplasty (PTCA), the efficacy of coronary stenting in acute ischemic syndromes remains unknown.