Release of interleukin-6 in acute myocardial infarction: apparent difference between myocardial necrosis and stunning

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Background: Elevated plasma levels of C-Reactive Protein (CRP) and Interleukin-6 (IL-6; the cytokine mainly responsible for CRP synthesis by the liver) have been demonstrated in patients with acute myocardial infarction (AMI). Plasma CRP has been correlated with infarct size, whilst IL-6 has been associated with myocardial stunning.

Methods: To assess whether CRP and IL-6 are related to infarct size, myocardial stunning or both, we measured the cumulative release of CRP and IL-6 during the first 48 hours in 44 patients with first AMI. Infarct size was assessed enzymatically (72-hours cumulative LDH release) and by 2D-echocardiography using wall motion score (WMS) at admission and at 3 months. Myocardial stunning was defined as change in WMS and number of segments showing reduction of systolic function from baseline to 3 months follow-up.

Results: Release in 48 hours (n = 44):

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<th>CRP (mg/L)</th>
<th>IL-6 (µg/L)</th>
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<tr>
<td>&lt;6</td>
<td>56</td>
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<td>&gt;6</td>
<td>&lt;56</td>
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<td>&gt;56</td>
<td>&lt;208</td>
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Mean WMS (admission): 7.1
Mean WMS (3 months): 3.2
Change WMS (adm-3 months): 0.9

Conclusion: IL-6 and CRP release in first AMI are positively correlated with infarct size. Myocardial stunning is more apparent in both the low IL-6 and CRP release groups.

Decreased levels of beta-endorphin in circulating mononuclear leukocytes from patients with acute myocardial infarction

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Objective: Beta-adrenergic stimulation and interleukin-1 activate lymphocytes and result in antinociception. Since both catecholamines and cytokines are elevated in acute coronary syndromes, we investigated levels of immunoreactive beta-endorphin in peripheral blood mononuclear cells from patients with acute myocardial infarction.

Methods: From 11 patients with acute myocardial infarction forearm venous blood samples were taken on admission and after 6, 12, 24, and 48 hours for routine laboratory measurements and peripheral blood mononuclear leukocyte preparations. Mononuclear leukocytes were counted, pelleted and homogenized; beta-endorphin was measured in supernatants by radioimmunoassay.

Results: Concentrations of immunoreactive beta-endorphin in mononuclear leukocytes at admission were 30±2 µg/g per 10^6 cells and decreased significantly to 6.9±1.9 µg/g per 10^6 cells after 48 hours (p<0.05). Concomitantly plasma levels of C-reactive protein gradually increased from the normal range at admission to 12.4±1.74 mg/dl at 48 hours. An inverse correlation was found between cell-associated immunoreactive beta-endorphin and C-reactive protein in acute myocardial infarction patients.

Conclusion: The decrease of beta-endorphin in peripheral blood mononuclear cells from patients with acute myocardial infarction is associated with increased risk of in-hospital coronary events.

Vascular endothelial growth factor mRNA synthesis by peripheral blood mononuclear cells in patients with acute myocardial infarction

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Vascular endothelial growth factor (VEGF) is an angiogenic glycoprotein that is upregulated in cardiac myocyte subjected to ischemia. Serum levels of VEGF are reportedly elevated in the subacute phase of acute myocardial infarction (AMI). However, there is no direct evidence that VEGF mRNA is expressed in patients with AMI. To investigate whether VEGF mRNA is expressed in AMI, we measured levels of VEGF mRNA in peripheral blood mononuclear cells (PBMC) obtained from patients with AMI using competitive polymerase chain reaction (PCR).

Results: Fifteen patients with AMI and 15 healthy controls were enrolled. PBMC were isolated from all patients on day 14 after onset, and from all controls. Total RNA was extracted from PBMC and reverse transcribed into cDNA. We performed competitive PCR by co-amplifying serial dilutions of GAPDH mutant templates containing a unique Eco RV site. To measure VEGF cDNA semiquantitatively in the samples containing identical amount of GAPDH, we performed competitive PCR similarly by co-amplifying serial dilutions of VEGF mutant templates containing a unique Eco RV site. We measured VEGF mRNA by Southern blot and densitometry. Sera were also obtained from the same patients on day 14 after onset, and the serum concentration of VEGF was measured by ELISA method.

Conclusions: Levels of VEGF mRNA in PBMC were elevated in the subacute phase of AMI and significantly correlated with serum VEGF concentration.

Results suggest that VEGF in PBMC is overexpressed in response to some signals during the subacute phase of AMI for the purpose of angiogenesis and healing.