Reduction of Myocardial Infarct Size by a HMG CoA-Reductase Inhibitor in Normocholesterolemic Rats

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Background: In addition to their lipid lowering properties, statins improve endothelial function by increasing the activity of endothelial nitric oxide synthase (eNOS). We hypothesized, that by this mechanism statins may protect the myocardium from ischemic injury.

Methods: Atherosclerotic rats underwent 30 min of coronary artery occlusion (CAO) followed by 180 min of reperfusion. Heart rate and arterial blood pressure were continuously monitored throughout the experiments. Plasma cholesterol concentrations were determined at the end of the experiments. Infarct size was measured by TTC staining and expressed as percentage of area at risk. Myocardial eNOS activity was measured by arginine to citrulline conversion assay. The rats were pretreated for one week either with cerivastatin (0.3 mg/kg/d) or placebo. In one set of experiments L-NAME (15 mg/kg), an inhibitor of eNOS, was administrated 15 min prior to CAO. Results: Cerivastatin increased myocardial eNOS activity by 58% (21 ± 1 to 33 ± 2 pmol/mg/min, p<0.05) and decreased infarct size by 49% (29 ± 7 % to 15 ± 5 %, p<0.05) without affecting hemodynamics or plasma cholesterol levels. Cardioprotection and upregulation of eNOS activity were abolished in rats co-treated with L-NAME. Conclusion: Thus, we conclude that a novel antagonist of both GP IIb/IIIa and vitronectin receptors attenuates platelet aggregation and the worsening of the severity of myocardial ischemia caused by the inhibitor of adenosine receptors. There appears the linkage between the signals of adenosine receptors and GP IIb/IIIa or vitronectin receptors in platelet or coronary endothelial cells.

Early Microvascular Reflow Status After Infarct Reperfusion Determines Outcome of Postinfarction Remodeling Independent of Myocardial Salvage


Background: Prompt opening of the infarct related artery is the treatment of choice for acute myocardial infarction (MI). A beneficial effect on left ventricular (LV) function often results even in patients in which little myocardium is salvageable. We hypothesized that this phenomenon is dependent on adequate early microvascular perfusion, METHODOLOGY: Six sheep were subjected to 1 hour of ischemia followed by reperfusion (group 1). Six sheep underwent 6 hours of ischemia followed by reperfusion (group 2) and 7 sheep were infarcted without reperfusion (control). The ischemic region in all animals was 23% of the LV mass at the apex. Microvascular reflow was studied using LV long axis real time contrast echocardiography and microsphere injections during coronary occlusion and after 2, 5, and 8 weeks. Echocardiography was used to assess changes in LV size and regional function throughout the study period. RESULTS: During coronary occlusion all animals demonstrated complete microvascular ischemia. After 30 minutes of coronary reperfusion, group 1 animals demonstrated microvascular reflow of the area at risk while group 2 animals demonstrated complete transmural non-reflow. At 2 weeks, both groups demonstrated complete return of transmural microvascular blood flow that persisted throughout the remainder of the study. Control animals never achieved reflow in the infarct region. The area at risk remained akinetic in all groups throughout the study. At eight weeks LV end-systolic volume increased by 134% in control animals and by 114% in group 2 but was unchanged in group 1. CONCLUSION: Early microvascular reflow dramatically improves post-infarction LV remodeling independent of myocardial salvage.