Rising Levels of CRP and PAI-1 After Plaque Disruption Are Associated with Thrombosis

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Introduction: Elevated levels of C-reactive protein (CRP) and plasminogen activator inhibitor-1 (PAI-1) have been associated with an increased risk of thrombosis. This study was conducted to determine the time between different interaction among CRP, PAI-1 and plaque disruption leading to thrombosis. Methods: A model of plaque disruption and thrombosis was used. Atherococlusis was induced in 16 NZW rabbits by balloon intramural injury and a high cholesterol diet for 6 months. Five normal rabbits were used as control. Serum samples were obtained from time course assays using control and atherosclerotic rabbits at 6, 12, 24, 36, 48, 60 and 72 hr after thrombus triggering with Russell viper venom and histamine and then sacrificed. Rabbit specific high sensitivity ELISA was developed to detect serum CRP and PAI-1 levels. Immunohistochemical staining for tissue factor was performed at sites of thrombosis and adjacent arterial sites. Results: Serum CRP levels increased starting at 12 hr and peaked at 36 hr (0.34 mg/dl) while serum PAI-1 levels peaked after 24 hr (3.5 mg/ml) following thrombus-triggering in atherosclerotic rabbits. CRP and PAI-1 levels did not rise in control rabbits. At postmortem, thrombi were detected only in rabbits that had higher CRP levels (0.34 = 0.19 vs. 0.11 = 0.07 mg/dl, p < 0.01). Tissue factor was prominently noted at sites that had thrombus and absent from adjacent arterial sites. Conclusion: The rise in rabbit serum CRP and PAI-1 as early as 12 to 24 hr after thrombus-triggering may indicate a potential use as immediate short-term risk markers for thrombosis. The time factor in CRP and PAI-1 rise could be helpful in clinical assessment of evolving cardiovascular events.

Inhibitory Effect of NF-κB Decay Oligodeoxynucleotides (ODN) on Neointimal Hyperplasia in the Rabbit Vein Graft Model

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As autologous veins remains the commonly used conduit for bypass grafts, neointimal hyperplasia is known to be one of the major disease processes in vein graft failure. We have focused on the important role of NF-κB, which controls the expression of numerous genes involved in various cytokines and adhesive molecules in vascular diseases. Indeed, we already reported that the suppression of NF-κB activation by NF-κB decoy ODN induced apoptosis of VSMCs and protected various stress-induced endothelial cell death in vivo. In this study, we focused on the effects of NF-κB decoy ODN or inhibition of restenosis after graft implantation using vein graft of rabbit hypercholesterolemic model. Jugular vein to carotid artery interposition grafts in rabbits were treated intraoperatively with NF-κB decoy ODN (40 mmol/L) or ex vivo pressure-mediated intimalization (300mmHg, 10min). At 4 weeks after vein implantation, histological staining demonstrated that the treatment with NF-κB decoy ODN significantly suppressed intimal hyperplasia as compared to scrambled decoy ODN (scribbled decoy: 3.83 ± 0.50 mm², NF-κB decoy: 1.79 ± 0.19 mm², p < 0.001). Media thickness of NF-κB decoy ODN-treated grafts was significantly increased (p < 0.005), leading to a significant reduction in intima-media ratio in the graft transfected with NF-κB decoy ODN as compared to scrambled decoy ODN (scribbled decoy: 1.48 ± 0.27, NF-κB decoy: 0.44 ± 0.06, p < 0.001). Vascular reactivity study demonstrated that the grafts transfected with NF-κB decoy ODN significantly improved the endothelium-mediated vasorelaxation as compared to scrambled decoy ODN (p < 0.005). Therefore, these data suggested that the inhibition of NF-κB activation using decoy ODN inhibited the development of neointimal hyperplasia in rabbit vein graft. Therefore, this strategy would be useful to reduce vein graft failure.

Inflammatory Markers CD40L, IL-6, Neopterin, and CRP Are Not Influenced by Homocysteine-Lowering Therapy in Patients with Coronary Artery Disease


Purpose: Inflammation is an important part of atherosclerotic. Homocysteine is established as an independent risk factor in occlusive vascular disease. Furthermore, independent of plasma total homocysteine, vitamin B12 is also associated with the risk of vascular disease. The precise underlying mechanism of these associations is, however, unknown. Several clinical trials are investigating whether lowering Hcy can prefer or halt the development of atherosclerosis. We tested the effects of homocysteine lowering B-vitamin therapy in the Western Norway