P18 CELECOXIB RESTORE ENDOTHELIAL FUNCTION IN HYPERCHOLESTEROLEMIC RABBITS

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ABSTRACT

Abnormalities in endothelium dependent arterial relaxation develop early in atherosclerosis/hypercholesterol. Prostaglandins and their metabolic precursors by cyclooxygenase enzyme (COX) are involved in the regulation of endothelial function and inflammatory process which is an important component of atherosclerotic plaque development. COX exists in two isoforms, COX-1 being responsible for physiological prostanoid synthesis, and COX-2 associated with proinflammatory cytokines. We investigated the effect of selective cox-2 inhibitor, celecoxib, on endothelium-dependent vasodilation in hypercholesterolemic rabbits. Rabbits were fed diet containing no additive (control), 1%cholesterol (cholesterol group) or 1% cholesterol with 30 mg/kg/day celecoxib (celecoxib group). After 12 weeks, endothelium-dependent vascular relaxations were assessed in isolate aortic rings and urinary nitrate excretions were assessed in 4 weeks interval. Acetylcholine- and ADP-mediated endothelium-dependent relaxations were significantly impaired in the cholesterol group, but preserved in the celecoxib group. Cholesterol feeding significantly reduced urinary nitrate excretion, urinary 6-keto PGF2 and increased urinary 8-iso PGF excretion. Treatment with celecoxib has no effect on plasma total-, LDL-, or HDL-cholesterol and urinary nitrate excretion but significantly reduced urinary 8-iso PGF excretion and restored urinary 6-keto PGF2 level to the control group. These data indicate that dietary treatment with selective COX-2 inhibitor, celecoxib, preserves endothelial vasodilator function in cholesterol-fed rabbits.