Salvianolic acid B attenuates cyclooxygenase-2 expression in vitro in LPS-treated human aortic smooth muscle cells and in vivo in the apolipoprotein-E-deficient mouse aorta.

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摘要

Abstract

Inflammation plays an essential role in atherosclerosis and post-angioplasty restenosis and the synthesis and release of inflammatory cytokines from vascular smooth muscle cells is an important contributor to these pathologies. It is assumed that drugs that prevent the overproduction of inflammatory cytokines may inhibit cardiovascular disorders. In the present study, the effects of a water-soluble antioxidant, salvianolic acid B (Sal B), derived from a Chinese herb, on the expression of cyclooxygenase (COX) in lipopolysaccharide (LPS)-treated human aortic smooth muscle cells (HASMCs) and in the aortas of cholesterol-fed apoE deficient mice were investigated. In unstimulated HASMCs, COX-2 mRNA and protein were almost undetectable, but were strongly upregulated in response to LPS. In contrast, HASMCs with or without LPS treatment showed constitutive expression of COX-1 mRNA and protein. The activation of COX-2 protein synthesis in LPS-stimulated HASMCs was shown to involve the activation of the extracellular-signal-regulated kinase 1/2 (ERK1/2), c-Jun NH(2)-terminal kinase (JNK), and p38 mitogen-activated protein kinase pathway. Incubation of HASMCs with Sal B before LPS stimulation resulted in pronounced downregulation of COX-2 expression. Sal B treatment suppressed ERK1/2 and JNK phosphorylation and attenuated the increase in prostaglandin E(2) production and NADPH oxidase activity in LPS-treated HASMCs. When apoE-deficient mice were fed a 0.15% cholesterol diet with or without supplementation with 0.3% Sal B for 12

weeks, the intima/media area ratio in the thoracic aortas was significantly reduced in the Sal B group (0.010 +/- 0.009%) compared to the apoE-deficient group (0.114 +/- 0.043%) and there was a significant reduction in COX-2 protein expression in the thickened intima. These results demonstrate that Sal B has anti-inflammatory properties and may explain its anti-atherosclerotic properties. This new mechanism of action of Sal B, in addition to its previously reported inhibition of LDL oxidation, may help explain its efficacy in the treatment of atherosclerosis.