alpha-Melanocyte-Stimulating Hormone Gene Transfer Attenuates Inflammation after Bile Duct Ligation in the Rat

林家瑋

Wang CC;Lin JW;Lee LM;Lin CM;Chiu WT;Pai HT;Hung KS

摘要

Abstract

Cholestasis occurs in a wide variety of human liver diseases, and hepatocellular injury is an invariant feature of cholestasis causing liver dysfunction and inflammation, promoting fibrogenesis, and ultimately leading to liver failure. alpha-Melanocyte-stimulating hormone (alpha-MSH) is a potent anti-inflammatory agent in many models of inflammation, suggesting that it inhibits a critical step common to different forms of inflammation. The aim of this study was to investigate whether the gene transfer of alpha-MSH could attenuate hepatic inflammation after bile duct ligation in the rat. Studies were performed in bile duct-ligated (BDL) rats. Hydrodynamic-based gene transfection with alpha-MSH plasmid via rapid tail vein injection was performed 30 min after ligation of bile duct. The endpoints were studied as markers of inflammation 7 days after bile duct ligation. alpha-MSH expression in liver via a single administration of naked plasmid was demonstrated. Liver inflammation index, including neutrophil infiltration and serum alanine aminotransferase, were significantly reduced in alpha-MSH gene transfer rats. Markers for liver inflammation, including expression of tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta), and inducible NO synthase (iNOS) mRNA, as assessed by real-time PCR, were also attenuated by alpha-MSH gene therapy. Expression of iNOS protein in liver diminished after alpha-MSH gene transfer. Consistent with these data, hepatic stellate cells (HSC) and Kupffer cells were markedly inhibited in alpha-MSH gene-treated rats. Our findings show that gene transfer of alpha-MSH could attenuate hepatic inflammation after bile duct ligation in the rat.