Effects of hypolipidemic agent nordihydroguaiaretic acid on lipid droplets and hepatitis C virus.


Source

Department of Medicine, Division of Infectious Disease, University of California, San Diego, La Jolla, CA.

Abstract

Hepatitis C virus (HCV) relies on host lipid metabolic pathways for its replication, assembly, secretion, and entry. HCV induces de novo lipogenesis, inhibits β-oxidation, and lipoprotein export resulting in a lipid-enriched cellular environment critical for its proliferation. We investigated the effects of a hypolipidemic agent, nordihydroguaiaretic acid (NDGA), on host lipid/fatty acid synthesis and HCV life cycle. NDGA negated the HCV-induced alteration of host lipid homeostasis. NDGA decreased sterol regulatory element binding protein (SREBP) activation and enhanced expression of genes involved in β-oxidation. NDGA inhibited very low-density lipoprotein (VLDL) secretion by affecting mediators of VLDL biosynthesis. Lipid droplets (LDs), the neutral lipid storage organelles, play a key role in HCV morphogenesis. HCV induces accumulation and perinuclear distribution of LDs, whereas NDGA most notably reduced the overall number and increased the average size of LDs. The antiviral effects of NDGA resulted in reduced HCV replication and secretion. Conclusion: NDGA-mediated alterations of host lipid metabolism, LD morphology, and VLDL transport appear to negatively influence HCV proliferation. (HEPATOLOGY 2011;).

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PMID:
21858850