Abstract

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L-carnitine prevents metabolic steatohepatitis in obese diabetic KK-Ay mice.


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AIM: Pharmacological treatment for metabolic syndrome-related nonalcoholic steatohepatitis (NASH) has not been established. Here, we investigated the effect of L-carnitine, an essential substance for β-oxidation, on metabolic steatohepatitis in mice.

METHODS: Male KK-Ay mice were fed a high-fat diet (HFD) for 8 weeks, with supplementation of L-carnitine (1.25 mg/ml) in drinking water for the latter 4 weeks.

RESULTS: Serum total carnitine levels were decreased following HFD-feeding, whereas the levels were reversed almost completely by L-carnitine supplementation. In mice given L-carnitine, exacerbation of hepatic steatosis and hepatocyte apoptosis was markedly prevented even though HFD-feeding was continued. Body weight gain, as well as hyperlipidemia, hyperglycemia and hyperinsulinemia, following HFD-feeding were also prevented significantly in mice given L-carnitine. HFD-feeding elevated hepatic expression levels of carnitine palmitoyltransferase 1A (CPT1A) mRNA; however, production of β-hydroxybutyrate in the liver was not affected by HFD alone. In contrast, L-carnitine treatment significantly increased hepatic β-hydroxybutyrate contents in HFD-fed mice. L-carnitine also blunted HFD-induction in sterol regulatory element binding protein-1c (SREBP1c) mRNA in the liver. Further, L-carnitine inhibited HFD-induced serine phosphorylation of insulin receptor substrate (IRS)-1 in the liver. L-carnitine decreased hepatic FFA contents in 1 week, with morphological improvement of swollen mitochondria in hepatocytes, and increases in hepatic ATP contents.

CONCLUSIONS: L-carnitine ameliorates steatohepatitis in KK-Ay mice fed an HFD, most likely through facilitating mitochondrial β-oxidation, normalizing insulin signal, and inhibiting de novo lipogenesis in the liver. It is therefore postulated that supplementation of L-carnitine is a promising approach for prevention and treatment of metabolic syndrome-related NASH.

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