Resveratrol and fenofibrate ameliorate fructose-induced nonalcoholic steatohepatitis by modulation of genes expression

Samira Mostafa ,Enas A Abd El-Haleim, Ashraf K Bahgat, Samira Saleh

Abstract

Abstract
AIM: To evaluate the effect of resveratrol, alone and in combination with fenofibrate, on fructose-induced metabolic genes abnormalities in rats.
METHODS: Giving a fructose-enriched diet (FED) to rats for 12 wk was used as a model for inducing hepatic dyslipidemia and insulin resistance. Adult male albino rats (150-200 g) were divided into a control group and a FED group which was subdivided into 4 groups, a control FED, fenofibrate (FENO) (100 mg/kg), resveratrol (RES) (70 mg/kg) and combined treatment (FENO + RES) (half the doses). All treatments were given orally from the 9th week till the end of experimental period. Body weight, oral glucose tolerance test (OGTT), liver index, glucose, insulin, insulin resistance (HOMA), serum and liver triglycerides (TGs), oxidative stress (liver MDA, GSH and SOD),serum AST, ALT, AST/ALT ratio and tumor necrosis factor-Ŭ (TNF-Ŭ) were measured. Additionally, hepatic gene expression of suppressor of cytokine signaling-3 (SOCS-3), sterol regulatory element binding protein-1c (SREBP-1c), fatty acid synthase (FAS), malonyl CoA decarboxylase (MCD), transforming growth factor-ƃ1 (TGF-ƃ1) and adipose tissue genes expression of leptin and adiponectin were investigated. Liver sections were taken for histopathological examination and steatosis area were determined.
RESULTS: Rats fed FED showed damaged liver, impairment of glucose tolerance, insulin resistance, oxidative stress and dyslipidemia. As for gene expression, there was a change in favor of dyslipidemia and nonalcoholic steatohepatitis (NASH) development. All treatment regimens showed some benefit in reversing the described deviations. Fructose caused deterioration in hepatic gene expression of SOCS-3, SREBP-1c, FAS, MDA and TGF-ƃ1 and in adipose tissue gene expression of leptin and adiponectin. Fructose showed also an increase in body weight, insulin resistance (OGTT, HOMA), serum and liver TGs, hepatic MDA, serum AST, AST/ALT ratio and TNF-Ŭ compared to control. All treatments improved SOCS-3, FAS, MCD, TGF-ƃ1 and leptin genes expression while only RES and FENO + RES groups showed an improvement in SREBP-1c expression. Adiponectin gene expression was improved only by RES. A decrease in body weight,HOMA, liver TGs, AST/ALT ratio and TNF-Ŭ were observed in all treatment groups. Liver index was increased in FENO and FENO + RES groups. Serum TGs was improved only by FENO treatment. Liver MDA was improved by RES and FENO + RES treatments. FENO + RES group showed an increase in liver GSH content.
CONCLUSION: When resveratrol was given with half the dose of fenofibrate it improved NASH-related fructose-induced disturbances in gene expression similar to a full dose of fenofibrate.
Key words: Fructose; Nonalcoholic steatohepatitis; Suppressor of cytokine signaling-3; Sterol regulatory element binding protein-1c; Fatty acid synthase; Malonyl CoA decarboxylase; Leptin; Adiponectin; Transforming growth factor-ƃ; Tumor necrosis factor-Ŭ

World J Gastroenterol 2016 March 14; 22(10): 2931-2948 2017, October