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Evaluation of circulating zonulin as a potential marker in the pathogenesis of nonalcoholic fatty liver disease.

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Abstract

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of liver disorders ranging from simple hepatic steatosis up to nonalcoholic steatohepatitis (NASH) evolving to cirrhosis and hepatocellular carcinoma (HCC). Liver biopsy is still the gold standard modality for diagnosing and staging NAFLD. The linkage between intestinal microbiota and NAFLD, might suggest a potential role of serum zonulin in NAFLD diagnosis. To appraise the role of circulating zonulin in NAFLD pathogenesis, 56 subjects with proved NAFLD by ultrasonography and liver biopsy, as well as 20 healthy controls were tested. Liver function tests, serum glucose, fasting insulin, C peptide, lipid profile, homeostasis model assessment of insulin resistance (HOMA-IR), IL-6, and circulating zonulin were performed to all subjects. Aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), triglycerides, HDL-c, fasting insulin, C peptide, HOMA-IR, IL-6, and serum zonulin were higher in NAFLD group than in controls ($p < 0.05$), and in NASH patients than those with simple steatosis ($p < 0.05$). Zonulin was positively correlated with body mass index (BMI), ALT, triglycerides, fasting insulin, HOMA-IR, liver histopathology, and serum IL-6 ($p < 0.05$), with inverse correlation to HDL-C ($p < 0.05$). At cut off 8.3 pc/mL, serum zonulin was found to be of diagnostic value of NASH occurrence with 100% sensitivity and specificity (AUR = 1.000, p-value = <0.001). The increasing zonulin levels in NAFLD patients with steep rise in NASH group denotes a possible role in pathogenesis of NAFLD occurrence and progression. This could open a new avenue of implicating zonulin antagonists as targeted therapies in NAFLD prevention.

KEYWORDS: IL6; NAFLD; NASH; Zonulin

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