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Huseyin Kayadibi

Hitit University, Turkey

The role of intestinal microbiota in the pathogenesis of non-alcoholic Steatohepatitis

Nonalcoholic Steatohepatitis (NASH) is determined as the fatty liver with inflammation and fibrosis that resembles the alcoholic liver disease without the history of alcohol ingestion. Genetic and environmental factors are important in the pathogenesis of NASH. However, it is still unclear why some lean individuals develop NASH, while some obese individuals do not. Intestinal microbiota may be important for the explanation of these situations. Because, microorganisms have some effects on energy homeostasis, activation of pro-inflammatory mediators, and metabolism of bile acids, short chain fatty acids, choline and alcohol.

Intestinal barrier components, tight junction, zonula adherence, desmosome, gap junction, integrin, selectin and cell adhesion molecule, have very important roles in the gut-liver axis for healthy liver. Because, intestinal barrier dysfunction causes the increased transfer of toxic metabolites to the liver from gut by the gut-liver axis. Increased levels of these substances in liver induce the multiple inflammatory processes by the activation of toll like receptors and nod like receptors that may result with the hepatitis and fibrosis.

Microbial imbalance called dysbiosis may cause to the development of leaky gut, and then NASH. In previously published articles, it was shown that intestinal dysbiosis and NASH are related with the lower prevalence of Bacteroidetes and higher prevalence of Firmicutes. Therefore, the species of microbiota may be important for elucidation of the pathogenesis of NASH. It was also shown that diversity of the intestinal microbiota has a key role for the pathogenesis of liver diseases. In future, studies with liver biopsy proven NASH patients will elucidate the role of intestinal microbiota and related metabolic components in the pathogenesis of NASH.

Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent public health problems. NAFLD encompasses the clinical course from simple fatty liver to non-alcoholic steatohepatitis (NASH), cirrhosis and hepatocellular carcinoma. NASH is an asymptomatic fatty liver with inflammation and fibrosis that resembles the alcoholic liver disease without the history of alcohol ingestion (1). The gold standard diagnostic tool used for the diagnosis of NASH today is the liver biopsy. Many biochemical markers have been investigated to use instead of the liver biopsy, but it has not been accomplished yet. Since microorganisms have some effects on energy homeostasis, activation of pro-inflammatory mediators, and metabolism of bile acids, short chain fatty acids, choline and alcohol, there has been an increase in studies about the role of microbiota in NAFLD and NASH (2).

Pathogenesis: Multiple parallel hits hypothesis is commonly accepted for the evaluation of inflammation in NAFLD (3). Intestinal microbiota is one of the components in this hypothesis. In healthy individuals, intestinal barrier components such as tight junctions, zonula adherence, desmosomes, gap junctions, integrins, selectin and cell adhesion molecules do not permit the transfer of toxic metabolites to the portal blood flow. In cases of intestinal barrier dysfunction, transfer of toxic metabolites in to the portal blood flow and then liver increases by the gut-liver axis. As a result, increased levels of these substances in liver induce the multiple inflammatory processes by the activation of toll-like receptors and nod like receptors that may result in hepatitis and fibrosis (4). Therefore, elucidation of the common microbiota species in healthy individuals and in patients with NASH may be useful for the pathogenesis of the NASH, as well as to elucidate why some lean patients develop NASH and why some obese patients don't.

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Gut Microbiome Composition in Patients with NASH Studies have shown that gut microbiome composition is very important for the development of NAFLD, but there are some conflicting results in published studies due to the use of different study designs and diagnostic methods. Therefore, standardization of study procedures is very important to compare the results correctly. In patients with NAFLD, lower proportions of Bacteroidetes, Prevotellaceae and Ruminococcaceae, and higher proportions of Porphyromas, Firmicutes, Proteobacteria and Fusobacteria were observed when compared with healthy individuals (5, 6). In comparison to the control group, low abundance of Ruminococcaceae and Faecalibacterium prausnitzii and high abundance of Lactobacillus, Escherichia and Streptococcus have also been shown in patients with NAFLD (7). It was also shown that patients with NASH had the lower intestinal microbiota diversity than healthy individuals.

Conclusion: Patients with NASH and heathy individuals have the varying intestinal microbiota composition. Comparison of the healthy individuals with liver biopsy proven patients with NASH or comparison of the lean and obese individuals with liver biopsy proven NASH may elucidate the role of intestinal microbiota and related metabolic components in the pathogenesis of NASH.

Biography

Huseyin Kayadibi has completed his Degree in Medicine at the Gülhane Military Medical Academy-School of Medicine, Turkey in 2000. He is an Associate Professor in Medical Biochemistry at Hitit University School of Medicine, where he is the Head of Medical Biochemistry. He worked at Pasarow Mass Spectrometry Laboratory, University of California Los Angeles in 2012 as a Visiting Scholar. He has been a Co-Investigator on NIH and other international projects about metabolomic, proteomic and lipidomic analysis. He is the Member of EFLM Working Group test evaluation and IFCC Working Group cerebrospinal fluid proteins. He has published more than 70 papers in peer reviewed journals. His research interests are Non-Invasive Assessment of Steatohepatitis, Liver Fibrosis, Separation Techniques and Mass Spectrometry.

mdkayadibi@yahoo.com

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