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Short Notes on Pathophysiology of Non Alcoholic Fatty Liver Disease

John Levorse*

Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland, USA

Description

Non-alcoholic fatty liver disease (NAFLD) is a catch-all term for a type of chronic liver disease caused by substances other than alcohol. It is distinguished by excessive fat deposition in the hepatocytes, known as steatosis. Non-alcoholic fatty liver (NAFL), characterised by harmless liver cell steatosis, non-alcoholic steatohepatitis (NASH), and variable degrees of fibrosis upon liver biopsy, are the pathological processes involved in NAFLD. NAFLD is also linked to liver cirrhosis and hepatocarcinoma in clinical studies. Globally, the prevalence of NAFLD is around 25%, endangering adults' health while primarily affecting children and adolescents. The prevalence of NAFLD in Asia is approximately 29.62 percent, with an increasing trend. NAFLD was linked to more than one-third of the deaths associated with liver diseases and diabetes in the United States.

Pathogenic factors for NAFLD include dietary habits, cardiovascular disease, genetic polymorphisms in various genes, and so on. Patients are at risk of complications such as hypertension, atherosclerosis, and other diseases during the progression of NAFLD from liver steatosis to fibrosis. However, the specific pathogenesis of NAFLD has not been determined, and no NAFLD-targeting chemotherapeutic options have been approved. As a result, a safe and effective treatment option for NAFLD is desperately needed. According to recent reports, these potential action targets and therapeutic drugs are primarily concerned with metabolic disorders, steatosis, oxidative stress, inflammation, apoptosis [1-3] and fibrosis. Several therapeutic drugs with the potential to treat NAFLD have been identified, and targeted NAFLD treatment strategies are likely to be implemented.

The "two hits hypothesis" and "multiple hits hypothesis" were proposed in the previous report to explain the pathogenesis of NAFLD. According to the "two hits" theory, fatty acid accumulation is caused by imbalances in glucose and lipid metabolism. Fatty acids, as a critical toxic component in liver cells, can increase oxidative stress and inflammatory factors, causing hepatocyte damage, an important pathological stage of NAFLD. As a result, the first "hit" is linked to lipid metabolism disorders, which are characterised by insulin resistance and a drop in adiponectin, leptin, and other major adipocytokines. Steatosis, endoplasmic reticulum stress, oxidative stress, hepatocyte inflammation, and fibrosis are all associated with the second "hit."

The causal relationship between the first and second "impacts" has not been determined. The "multiple hits hypothesis" is thought to accurately explain the pathogenesis of NAFLD. Multiple factors, including insulin resistance, nutritional factors, oxidative stress, inflammatory factors, obesity, type 2 diabetes, hormones, gut microbiota, and epigenetic factors, are thought to contribute to NAFLD pathogenesis. Insulin resistance and liver-free fatty acids (FFA) are currently thought to play important roles in NAFLD pathogenesis. Excess FFA can enter the liver cells and be converted into triglycerides as a result of glucose and lipid metabolism disorders. Triglyceride accumulation in hepatocytes results in the formation of lipid droplets and the activation of NAFL.

Excess FFA also increases endoplasmic reticulum pressure, mitochondrial pressure, and the production of reactive oxygen species in the liver, resulting in inflammation, specifically NASH. NASH pathology includes portal vein and lobular inflammation, as well as hepatocyte injury. As NASH progresses, some hepatocytes undergo apoptosis or necrosis and produce inflammatory factors, which activate hepatic stellate cells [4,5] and cause liver fibrosis. Liver fibrosis is the abnormal expression and accumulation of extracellular matrix proteins in the liver, and it is a side effect of hepatitis that progresses to cirrhosis and liver cancer, necessitating a liver transplant for treatment. Tackling NAFLD-associated fibrosis from multiple angles with combination drug therapy and effective lifestyle changes has the best chance of success.

Liver fibrosis is the abnormal expression and accumulation of extracellular matrix proteins in the liver, and it is a side effect of hepatitis that progresses to cirrhosis and liver cancer, necessitating a liver transplant. Tackling NAFLD-associated fibrosis from multiple angles with combination drug therapy and effective lifestyle changes has the best chance of success. SGLT2 is primarily found in the proximal tubular curvature and is responsible for 80-90 percent of glucose re-absorption in the kidney. SGLT-2 inhibitors are glucose-lowering agents that promote weight loss and lower serum uric acid levels while improving glucose control. Several SGLT2 inhibitors, such as canagliflozin and dapagliflozin, were able to prevent lipid accumulation in the liver and lower levels of liver transaminase in clinical trials for the treatment of NAFLD patients by promoting urinary glucose excretion. NGI001, a novel selective SGLT2 inhibitor, was used to treat mice with high-fat diet (HFD)-induced nutritive obesity.

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None.

Conflict of Interest

The author declares that there is no conflict of interest associated with this paper.

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***Address for Correspondence:** John Levorse, Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland, USA, E-mail: Johnlev@yahoo.com.*

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