Role of oxidative stress and homocysteine in non-alcoholic fatty liver disease

Nikhil D Patel
Jivandeep Hospital, India

Nonalcoholic fatty liver disease (NAFLD), hepatic manifestation of metabolic syndrome is now the commonest chronic liver disease due to rising obesity and diabetes. NAFLD progresses from simple steatosis (NAFL) to steatohepatitis (NASH) and cirrhosis. In presence of suitable genetic and environmental factors (diet/physical activity/gut dysbiosis), insulin resistance (IR) and obesity results in adipose dysfunction, which triggers proinflammatory response, decreased lipolysis, increased de-novo lipogenesis and further increased IR. These events increase free fatty acid (FFA) flux to liver, which leads to triglyceride accumulation (NAFL). Toxic levels of FFA in liver trigger increased β-oxidation and mitochondrial dysfunction (MD). Obesity, homocysteine and environmental factors trigger endoplasmic reticulum stress (ERS). MD and ERS result in reactive oxygen species (ROS) production. ROS activates antioxidant mechanisms (consisting of enzymes like Superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione transferase; and non-enzymes like vitamin A, C, E, β-carotene and glutathione) which scavenges them, but over production of ROS results in depletion of antioxidants. Homocysteine adds to ROS production and suppresses antioxidants. Oxidative stress results in proinflammatory cytokine production, lipid peroxidation (measured by Malonildialdehyde) and protein adducts production leading to cell injury, inflammation and cell death leading to NASH. In addition, it triggers hepatic stellate cell activation leading to fibrosis and subsequently cirrhosis. Oxidative stress also produces DNA damage leading to future hepatocellular carcinoma. So, oxidative stress remains central to development of NASH and cirrhosis. In clinical practice, differentiating NAFL and NASH requires liver biopsy because non-invasive scoring systems are not sensitive. Measuring homocysteine and enzymes (like glutathione transferase, glutathione peroxidase, catalase, etc.) may prove helpful to define progress to NASH. Also targeting these molecules by newer therapeutic strategies may halt progression of NAFLD.

Speaker Biography

Nikhil D Patel (MD, DNB [Gastroenterology]) is practicing as a Consultant Gastroenterologist since 12 years. He has around 50 publications in various journals. He has presented more than 80 scientific papers in reputed conferences.

e: niyopatel@yahoo.com

Notes: