

Abstract #9

Is NASH triggered by a leaky gut?

Background: The pathophysiology of non-alcoholic fatty liver disease (NAFLD) has not been clearly delineated, but there appears to be a “two hit” mechanism, the initial insult being fatty acid accumulation in the liver, followed by another event which leads to inflammation and fibrosis. One of the proposed second hit mechanisms is oxidative stress. Studies in alcoholics and in obese rats have shown that bacterial lipopolysaccharide and endotoxin are the triggers for oxidative stress and subsequent steatohepatitis. Increased intestinal permeability due to disruption of the gut barrier function has been shown to be a source of endotoxemia and oxidative stress in alcoholics. We propose a similar mechanism in NAFLD.

Aim: We aim to determine whether patients with nonalcoholic steatohepatitis have intestinal hyperpermeability (leaky gut) and whether leaky gut can differentiate simple steatosis from non-alcoholic steatohepatitis (NASH) in obese patients.

Methods: Obese patients were recruited from the [redacted] surgery center or [redacted]. Steatosis and NASH were diagnosed by liver biopsy using Brunt criteria. Intestinal permeability was measured using urinary excretion of poorly absorbed sugars (a cocktail containing lactulose(L), sucrose(S), mannitol(M) and sucralose(Slc)). To determine whether patients had increased susceptibility to leakiness, the permeability test was repeated after aspirin challenge (1300mg ASA). Urinary sugars were measured by gas chromatography. Small bowel permeability was defined by the Lactulose/Mannitol (L/M) ratio and whole gut permeability was defined by sucralose excretion. Median values for sugar excretion were compared between all groups using Kruskal-Wallis and between each group using Mann-Whitney tests with Bon-Ferroni correction.

Results: There was no statistically significant difference between patients with steatosis (n=6) and NASH (n=10) in regards to age, presence of diabetes mellitus, body mass index, aspartate amino transferase(AST), alkaline phosphatase, total bilirubin, or cholesterol levels. Serum alanine amino transferase (ALT) levels were significantly higher in patients with NASH. (p=0.021). Small bowel permeability was similar between controls (n=12), steatosis and NASH. Similarly, total gut permeability was similar between all groups. However, patients with steatohepatitis had an increased susceptibility to whole gut permeability with aspirin challenge (p=0.033), suggesting that the colon is susceptible to leakiness in patients with NASH. In contrast, patients with simple steatosis had no increased susceptibility to leakiness with aspirin challenge.

Discussion: Our results confirm prior work that patients with steatohepatitis do not have increased gut permeability as compared to steatosis or controls at baseline. However, they do have an exaggerated response to aspirin challenge suggesting an increased susceptibility to gut leakiness. Therefore, avoidance of factors that may deleteriously affect intestinal permeability, such as non-steroidal anti-inflammatory medications, is strongly suggested in those at risk for NAFLD.

Pre and Post-ASA sucralose excretion in NASH vs. steatosis

