NASH AND NUTRITIONAL MANAGEMENT

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What is NASH?

- Nonalcoholic Steatohepatitis characterized by fatty liver, inflammation, and damage

- NASH develops in 2-5% of Americans (especially people who are middle-aged and overweight or obese)

- Often called “silent” liver disease (patients feel well in early stage). Fatigue, weight loss, and weakness occur once disease progresses or cirrhosis develops

- Resembles alcoholic liver disease (but occurs in people who drink little to no alcohol)
NASH vs. NAFLD

- Nonalcoholic Fatty Liver Disease (NAFLD) = The presence of fat in the liver without inflammation or damage.

- Diagnosing NASH:
  1. Elevated liver enzymes i.e. elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST).
  2. When medication use, viral hepatitis, and excessive alcohol usage have been ruled out, and X rays or imaging show fat in the liver, NASH is suspected.

The only way to diagnose NASH and differentiate it from NAFLD is a liver biopsy.
Pathogenesis

- Insulin resistance: Excess energy intake, obesity, and a combination of different genetic and environmental factors can lead to insulin resistance.

- Insulin resistance along with excess accumulation of free fatty acids (FFA) and intracellular formation of toxic lipid metabolites (in oxidative degradation of lipids) illicit an inflammatory response that triggers progression to NASH.

- Diet and exercise modifications are the best options for preventing the progression of NAFLD to NASH and for managing NASH once it develops.
Dietary Modifications and Lifestyle Changes in NASH

- Several studies show the beneficial effects of diet, weight loss, and exercise in NAFLD. These modifications can reduce insulin resistance and normalize ALT.

- Studies comparing the efficacy of different types of diets (i.e. traditional low fat vs. calorie restriction with low carbohydrate diet) in producing weight loss have not been able to prove the superiority of one over the other.
Dietary Modifications & Lifestyle Changes in NASH

- All studies support the fact that small degrees of weight loss of around 5–10% of the total body weight show a clear benefit.

- Changes in the amount of fat delivery to the liver related to dietary fats and subsequent alterations in lipid metabolism are as important as the actual weight loss. This would be an important point for clinicians to emphasize to NAFLD patients during weight loss counseling.

- Very rapid weight loss (generally >1.6 kg/week) may cause worsening of the inflammation with NASH, and accelerate progression of the disease by drastically increasing visceral adipose tissue breakdown and delivery to the liver.
Orlistat, antioxidants, and n-3’s

- **Orlistat**: Orlistat inhibits gastric and pancreatic lipase, resulting in reduced absorption of long chain fatty acids and cholesterol by 30% (unabsorbed fat is passed in stool). Statistically significant reduction in fatty liver as detected by ultrasound in comparison to non-orlistat patients in a study observing 44 patients in a double blind placebo controlled study.

INCONCLUSIVE:

- **Antioxidants in NAFLD**: Conchrane database meta-analysis observing six trials: The six trials used different combinations of antioxidants including selenium, vitamin C, and vitamin E to evaluate progression of NAFLD. Findings: Insufficient evidence to support or refute a role for these in NAFLD patients.

- **Omega-3 fatty acids and NAFLD**: No adverse events were reported in any of the studies exploring the relationship between omega-3’s and NAFLD. N-3 PUFA may have a role in management of NAFLD, but more studies are needed to confirm its benefit and define dosing and length of administration.
**HFCS and Trans-fats**

- **High-fructose corn syrup and trans-fatty acid in NAFLD**
  One recent study comparing the dietary patterns of 49 patients with NAFLD to 24 control patients with other types of chronic liver disease, found a two-fold higher consumption of HFCS among the NAFLD patients.

  *Increases in hepatic fat deposition in healthy patients consuming large amounts of HFCS has been proven by MR spectroscopy in a study using 16 healthy males with history of diabetes in parents vs. 8 control patients: ½ on high kcal, high HFCS diet and ½ on isocaloric diet for 7 days*

- **Trans-fats and NAFLD**: Animal studies have documented the role of trans-fatty acids in the pathogenesis of NAFLD and NASH. **No human studies** have observed this relationship yet.
Bariatric Surgery

- **Bariatric surgery**: Recent large meta-analysis of the effect of bariatric surgery on NAFLD and NASH included 15 studies with 766 total paired liver biopsies. A significant improvement in steatosis was observed in 91%; steatohepatitis improved in 81%. All patients had BMI >40 or >35 with co-morbidities.
Risk Factors for NAFLD

- Obesity, T2DM, and hyperlipidemia are recognized as risk factors for NAFLD. Many NAFLD patients also have insulin resistance.

- The number of patients with normal BMI and NAFLD is increasing. These individuals typically have central obesity, occult (unknown) insulin resistance, and unhealthy dietary composition.
Dietary Fats

- Triglycerides deposit in liver due to:
  1. Excessive influx of free fatty acids (FFA) from endogenous fat stores
  2. Increased hepatic lipogenesis
  3. Exogenous (dietary) fats

- Multiple studies in animals have documented that a high-fat diet rapidly induces hepatic steatosis (excess lipid accum.), but data in humans are scarce
Sugar, Soft Drinks, and NAFLD

- A sucrose-rich diet increases the hepatic synthesis of triglycerides. Rats and humans that are fed either sucrose- or fructose enriched diets develop fatty livers.

- Several studies have been published on the association between soft drinks consumption and NAFLD, demonstrating a positive association. The first was a cross-sectional study of a sub-sample (n = 375) of the Israeli National Health and Nutrition Survey (1999-2001). A semi-quantitative food-frequency questionnaire was administered and showed that NAFLD patients have a higher intake of soft drinks. Moreover, the higher intake of soft drinks was associated with an increased risk of NAFLD, independently of age, gender, BMI, and total calories.

- Physicians and dietitians should routinely include questions regarding soft-drink consumption as part of the patient’s history/advise pts against their consumption.
Citations

