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REVIEW ARTICLE

Emerging Pandemic and Silent Killer – Non Aloholic Fatty Liver Disease: A Comprehensive Review

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is quickly becoming one of the most prominent causes of liver disease worldwide. The increasing incidence of NAFLD is tied to the obesity epidemic and the subsequent metabolic derangements brought along with it. Current efforts to elucidate the mechanism and causes of the disease have answered some questions, but much remains unknown about NAFLD. The aim of this article is to discuss the current knowledge regarding the pathogenesis of the disease, as well as the current and future diagnostic, preventative, and therapeutic options available to clinicians for the management of NAFLD.

KEYWORDS

• Nonalcoholic fatty liver disease • Steatohepatitis • Nonalcoholic steatohepatitis • Pathogenesis • Treatments • Diagnosis • Management

INTRODUCTION

The problem of obesity has grown tremendously through the 20th century and into the 21st century, slowly transforming into an epidemic. Along with it, nonalcoholic fatty liver disease (NAFLD) has become one of the major diseases plaguing the nation and world. In the United States, NAFLD is the most common cause of liver disease, representing over 75% of the chronic liver disease. It also is one of the most common indications for liver transplantation, contributing a major burden to both the morbidity and mortality of the nation. NAFLD is a disease of all ages, and the disease has been reported in children as young as 2 years of age. The prevalence of fatty liver increases with age in adults, and while the exact incidence of the disease is unknown, In the

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United States National Health and Nutrition Examination Survey, 6% of overweight, and 10% of obese adolescents had an elevated alanine aminotransferase (ALT), although alcohol use was not excluded.[1]

Given the increasing prevalence of the disease, adequate knowledge regarding the disease is becoming especially important for physicians and patients. Despite this, since its description in 1980, nonalcoholic steatohepatitis (NASH) has been a difficult to understand and treat for both scientists and clinicians.[2]

The spectrum of NAFLD is a continuum ranging from simple steatosis to NASH and finally cirrhosis. The defining characteristic of the disease is the presence of greater than normal lipid deposition within the liver with the absence of excessive alcohol consumption defined as > 20 g/d for men and 10 g/d for women.[3]

PATHOGENESIS

Normal liver processing of lipid The liver is one of the principle regulators of lipid in the body (Figure 1). Fatty acids in the liver used for triglyceride (TG) synthesis are provided by diet, adipose tissue or *de novo* synthesis from excess glucose.[4]

Insulin resistance, frequently found in those with metabolic syndrome, obesity and/or diabetes, is frequently considered the key factor in developing hepatic steatosis. The progression of steatosis to NASH is a frequently encountered clinical scenario, associated with worse outcomes for patients. A key-defining feature of the NASH is the presence of inflammation and subsequent fibrosis. Change of concentration in several inflammatory cytokines has been implicated in this progression.[5]

DIAGNOSIS

Initial evaluation The diagnosis of NAFLD requires (1) there is hepatic steatosis by imaging or histology; (2) there is no significant alcohol consumption; (3) no competing etiologies are present for hepatic steatosis; and (4) there are no co-existing causes for chronic liver disease. Numerous attempts have been made at creating a noninvasive scoring model to assess fibrosis in NAFLD. The most extensively researched model is the NAFLD Fibrosis Score, which incorporates age, BMI, AST/ALT ratio, platelet count, and albumin. Incidental finding of hepatic steatosis is frequently found when a patient receives a CT. CT without contrast is a useful modality for assessing the presence and amount of steatosis, with a sensitivity ranging from 82% to 95% and a specificity approaching 100%.[6]

Magnetic resonance spectroscopy (MRS) represents the most sensitive and specific imaging modality, with both values being greater than 90% in most studies(93) and near 100% accuracy in detecting steatosis.

Liver biopsy - Currently, liver biopsy remains the gold-standard for the diagnosis of NASH as it serves as the only means of distinguishing hepatic steatosis from steatohepatitis through examination of liver histology.[7]

PREVENTION AND MANAGEMENT

Prevention While other interventions, such as alcohol consumption and dietary supplementation, have been suggested for disease prevention, at this time none are recommended by the AGA Furthermore, it is important to note that the use of preventative vaccines, such as the hepatitis A and B vaccines, is recommended in patients suffering from NAFLD and NASH, in order to prevent further insult to the already damaged liver.[8]

Lifestyle modifications The cornerstone to the management of steatosis and NASH to date has been lifestyle changes, with the two most central components being diet and exercise. Diet and exercise have been proposed as a treatment option for steatosis and NASH, however study data is limited to date. Studies have been held back by the lack of consensus in regards to the methodology used to determine whether the disease progressed or improved.[9]

Other studies have shown an improvement in the disease through exercise alone. Finally, studies have shown that diet and exercise have been successful in preventing steatosis progression to NASH. Currently the American Gastroenterology Association recommends both exercise and healthy weight loss, either separately or in combination therapy, as interventions for NASH. While both interventions are indicated from a general health perspective and from numerous studies, it is important to note that presently the Cochrane Review is unable to make a

recommendation regarding weight loss in NAFLD due to the lack of quality data at this time, highlighting the need for further research in the area.[10]

Alcohol use is another life style modification that has been investigated. While the deleterious effects of heavy alcohol use on the liver are well established, the moderate use of alcohol has been investigated in relation to NAFLD. A 2014 retrospective study demonstrated patients who were moderate alcohol users had a decrease in severity of disease histologically. Other studies have showed modest wine drinking was correlated with a decreased prevalence of NAFLD. Additionally comparison between nondrinkers and moderate drinkers with NAFLD demonstrated lower rates of steatohepatitis in the moderate drinkers. While some benefit may exist for moderate alcohol consumption, based on the data no recommendation can be made regarding alcohol consumption, other than heavy drinking should be avoided.[11]

Dietary supplementation - Antioxidant supplementation has been widely hypothesized to have benefits in patients with NASH, as oxidative stress is a central component to liver injury and damage. Vitamin E is perhaps the most well researched of the proposed antioxidants. It is important to note that studies have suggested that Vitamin E supplementation has been linked to an increase in all-cause mortality (although conflicting data has since been published), as well as prostate cancer. While these risks are low, it is important for clinicians consider these risks and discuss them with their patients before recommending Vitamin E.[12]

Caffeine and coffee use has also been linked to decreased fibrosis, decreased progression to steatohepatitis as well as decreased incidence of the disease amongst its users. On the other hand, a recent study demonstrated the protective effects of coffee in women with NAFLD, however the same effect was not observed in patients who used espresso. While this may suggest that coffee itself may have protective effect *vs* caffeine alone, further studies have found an increased activity of the autophagy-lysosomal pathways in mice fed caffeine, inferring a biochemical explanation for the protective role of caffeine.[13]

Several other supplements have also been suggested as treatment options for NAFLD, none currently embrace enough evidence to be recommended for widespread therapeutic use at this time. In a recent meta-analysis probiotics have been shown to lower aminotransferases, total cholesterol, TNFα and improve insulin resistance in NAFLD. Given the relatively benign nature of probiotics and their availability over the counter, clinicians should be aware of their potential benefit in NAFLD. Ursodeoxycholic acid has been demonstrated in numerous small studies to have a benefit on liver enzymes and other measurable outcomes, however larger studies did not demonstrate significant histologic improvement. Omega-3 fatty acids have also shown promise for treating NASH, several studies have shown measurable decreases in ALT and hepatic fat content in patients. However despite these trials, the efficacious dose has not been established, histopathologic data is sparse and high quality randomized controlled trials have not been done, although one is in process. High dose niacin therapy has also been shown to prevent steatohepatitis and liver deposition in rats, showing promise as a potential future therapeutic treatment modality with further research.[14]

Metformin Due to the link between insulin resistance and NAFLD, several studies have investigated the use of oral insulin sensitizing agents for the treatment of the disease. One of the most studied insulin sensitizing drugs is metformin. While several studies have demonstrated a decrease in ALT and increases in insulin sensitivity in patients with fatty liver, few have established histologic improvement. Another study established that metformin is less effective at decreasing liver enzymes and hepatic content than exercise alone; furthermore in a 2010 study, metformin was observed to have only a weak improvement over di*et al*one. In a study looking specifically at patients with insulin resistances, without diabetes, metformin was found to have little to no histopathologic improvement when compared to controls, however it should be noted that this study included small number of patients and had a significant dropout rate. Another study comparing metformin,[15] vitamin E and diet similarly showed no histologic difference, despite ALT improvement. While there is one small study showing histologic improvement in NASH patients following a 48 wk treatment period the inconclusive and conflicting evidence lead to the conclusion that

further investigations are necessary before recommending the use of metformin for NASH without coexisting diabetes.[16]

The cardiovascular manifestations of liver diseases, including NAFLD are commonly seen and contribute significantly to the morbidity and mortality of liver disease patients.[17] Statins are a commonly prescribed preventative treatment for patients with cardiovascular risk factors and disease. The use of statins in patients with liver disease including NAFLD has been established as safe and can be used in the treatment of cardiovascular disease in these patients. The use of statins as a therapy targeted specifically at NASH has shown promise in recent studies.[18] The results have been mixed, with one early study showing no improvement in serologic markers, and other studies showing benefit.[19]

Treatments for NASH in children do not differ significantly from those recommended for adults. Data has shown lifestyle modification is the mainstay of treatment.[20] The largest study of pharmacotherapy for NASH in children to date was the TONIC trial in 2011.[21] It demonstrated no difference in children between metformin or vitamin E and placebo, however the primary outcome of the study was reduction in ALT. When stratified for reduction in steatohepatitis in children with NASH, a 58% improvement was seen in the vitamin E treatment group ($P = 0.006$). The TZDs have not been investigated in children sufficiently for recommendation.[22]

CONCLUSION

Finally, NAFLD is a growing problem worldwide and with the increasing prevalence and incidence of obesity NAFLD could soon become an epidemic.[23] Despite the positive strides made over the last several years, much remains to be understood regarding the mechanism of the disease. Our incomplete understanding of the pathogenesis is a major hurdle in the path towards developing methods for preventing and treating the disease.[24] Additionally, the lack of awareness of the disorder and absence of reliable noninvasive diagnostic tools, has likely left many patients undiagnosed.[25] For these reasons, there is a pressing need for further research into developing additional diagnostic tools and therapeutic modalities. Until then, education regarding lifestyle modifications for at risk populations is imperative.[26] In NAFLD, as is the case in many diseases, an ounce of prevention is worth a pound of cure.

REFERENCES

1. Younossi Z.M., Stepanova M., Afendy M., Fang Y., Younossi Y., Mir H., Srishord M. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. Clin Gastroenterol Hepatol. 2011
2. Strauss R.S., Barlow S.E., Dietz WH. Prevalence of abnormal serum aminotransferase values in overweight and obese adolescents. J Pediatr. 2000; 136: 727–733.
3. Suzuki A., Angulo P., Lymp J., St Sauver J., Muto A., Okada T., Lindor K. Chronological development of elevated aminotransferases in a nonalcoholic population. Hepatology. 2005; 41: 64–71. doi: 10.1002/hep.20543.
4. Hamaguchi M., Kojima T., Takeda N., Nakagawa T., Taniguchi H., Fujii K., Omatsu T., Nakajima T., Sarui H., Shimazaki M., *et al*. The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. Ann Intern Med. 2005; 143: 722–728.
5. Whalley S., Puvanachandra P., Desai A., Kennedy H. Hepatology outpatient service provision in secondary care: A study of liver disease incidence and resource costs. Clin Med. 2007; 7: 119–124.
6. Sozio M.S., Liangpunsakul S., Crabb D. The role of lipid metabolism in the pathogenesis of alcoholic and nonalcoholic hepatic steatosis. Semin Liver Dis. 2010; 30: 378–390.
7. Ludwig J., Viggiano T.R., McGill D.B., Oh B.J. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease.
8. Cohen J.C., Horton J.D., Hobbs H.H. Human fatty liver disease: old questions and new insights. Science. 2011; 332: 1519–1523.
9. World Gastroenterology Organisation Global Guidelines. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis 2012.
10. Neuschwander-Tetri B.A. Nonalcoholic steatohepatitis and the metabolic syndrome. Am J Med Sci. 2005; 330: 326–335.
11. Argo C.K., Caldwell S.H. Epidemiology and natural history of non-alcoholic steatohepatitis. Clin Liver Dis. 2009.
12. Brown M.S., Goldstein J.L. The SREBP pathway: Regulation of cholesterol metabolism by proteolysis of a membrane-bound transcription

factor. Cell. 1997.

13. Yamashita H., Takenoshita M., Sakurai M., Bruick R.K., Henzel W.J., Shillinglaw W., Arnot D., Uyeda K. A glucose-responsive transcription factor that regulates carbohydrate metabolism in the liver. Proc Natl Acad Sci USA. 2001; 98: 9116.

14. Ma L., Robinson L.N., Towle H.C. ChREBP*Mlx is the principal mediator of glucose-induced gene expression in the liver. J Biol Chem. 2006;

15. Willy P.J., Umesono K., Ong E.S., Evans RM, Heyman R.A., Mangelsdorf D.J. LXR, a nuclear receptor that defines a distinct retinoid response pathway.

16. Huang Y., He S., Li J.Z., Seo Y.K., Osborne T.F., Cohen J.C., Hobbs H.H. A feed-forward loop amplifies nutritional regulation of PNPLA3. Proc Natl Acad Sci USA. 2010; 107: 7892–7897.

17. Cha J.Y., Repa J.J. The liver X receptor (LXR) and hepatic lipogenesis. The carbohydrate-response element-binding protein is a target gene of LXR. J Biol Chem. 2007; 282: 743–751. doi: 10.1074/jbc.M605023200.

18. Langin D. Adipose tissue lipolysis as a metabolic pathway to define pharmacological strategies against obesity and the metabolic syndrome. Pharmacol Res. 2006; 53: 482–491. doi: 10.1016/j.phrs.2006.03.009.

19. Hooper A.J., Adams L.A., Burnett J.R. Genetic determinants of hepatic steatosis in man. J Lipid Res. 2011; 52: 593–617. doi: 10.1194/jlr.R008896.

20. Bandsma R.H., Prinsen B.H., van Der Velden Mde S., Rake J.P., Boer T., Smit G.P., Reijngoud D.J., Kuipers F. Increased de novo lipogenesis and delayed conversion of large VLDL into intermediate density lipoprotein particles contribute to hyperlipidemia in glycogen storage disease type 1a. Pediatr Res.

21. Schwimmer J.B., Celedon M.A., Lavine J.E., Salem R., Campbell N., Schork N.J., Shiehmorteza M., Yokoo T., Chavez A., Middleton M.S., *et al*. Heritability of nonalcoholic fatty liver disease. Gastroenterology.

22. Hesham A. Kader H. Nonalcoholic fatty liver disease in children living in the obeseogenic society. World J Pediatr. 2009; 5: 245–254.

23. Browning J.D., Szczepaniak L.S., Dobbins R., Nuremberg P., Horton J.D., Cohen J.C., Grundy S.M., Hobbs H.H. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. Hepatology.

24. Bambha K., Belt P., Abraham M., Wilson L.A., Pabst M., Ferrell L., Unalp-Arida A., Bass N. Ethnicity and nonalcoholic fatty liver disease. Hepatology.

25. Speliotes E.K., Butler J.L., Palmer C.D., Voight B.F., Hirschhorn J.N. PNPLA3 variants specifically confer increased risk for histologic nonalcoholic fatty liver disease but not metabolic disease.

26. Romeo S., Kozlitina J., Xing C., Pertsemlidis A., Cox D., Pennacchio L.A., Boerwinkle E., Cohen J.C., Hobbs H.H. Gene.tic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease.