Current Treatment of Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis

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KEYWORDS

• NAFLD • NASH • Treatment • Pharmacotherapy

KEY POINTS

- Body weight loss via physical activity and dieting is the mainstay of treatment of nonalcoholic fatty liver disease (NAFLD).
- Bariatric and endoscopic weight loss surgery can be effective in obese patients with NAFLD, with and without metabolic complications.
- There is no currently approved pharmacotherapy; vitamin E and pioglitazone are available medications with the most evidence of efficacy in the treatment of patients with NAFLD but have side effects and limitations.
- Treatment of NAFLD should be individualized to each patient's comorbidities and unique situation.

The goal of treatment of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) is to stop the progression of hepatic inflammation and necrosis, which result in fibrosis, cirrhosis, and liver failure. It is also important to improve patient quality of life, the need for hospitalizations and health care utilization, and NAFLD-associated cardiovascular and metabolic complications. Therapy is directed toward patients with NASH. This is because those with NAFLD alone, without steatohepatitis, have a relatively benign course and good prognosis.[1] Currently there are no Food and Drug Administration–approved therapies for NAFLD/NASH. This article examines the role of lifestyle modifications, including diet and exercise, which are the

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mainstay of treatment. In addition, the role of weight loss surgery and available pharmacologic therapies is discussed.

LIFESTYLE MODIFICATIONS

Intentional weight loss via lifestyle modifications, through a combination of increased physical exercise and calorie-restricted dieting, is currently the mainstay of treatment of NAFLD and is recommended by the American Association for the Study of Liver Diseases and the American Gastroenterological Association.[1] Body weight loss of at least 3% to 5% is required before improvement in hepatic steatosis is seen.[2,3] Using improvement in histology as an endpoint, Promrat and coworkers showed a 2.4-point improvement in NASH fibrosis score (NAS)[4] in the successful weight loss group, from 4.4 at baseline to 2.[5] The amount of weight loss correlated with the degree of histologic improvement. The magnitude of weight loss correlates proportionally with NAS, especially when body weight loss is above 7%. A meta-analysis of 8 randomized clinical trials of weight loss, by Musso and coworkers,[6] confirmed that 7% weight loss resulted in improved NAS, with 2 other trials suggesting that 10% or more did not result in further benefit. Even though weight loss is effective in improving NAS, fewer than half of patients are able to achieve such goals.[6] Although hepatic steatosis, ballooning, lobular inflammation, and NAS are improved, these trials did not show improvement in hepatic fibrosis. A prospective cohort study by Vilar-Gomez and coworkers,[7] in 2015, confirmed that a weight loss of 7% to 10% improved NAS in 100% and steatohepatitis resolution in 90%. Fibrosis regression, in contrast to previous studies, was documented in 45% of those who were able to lose more than 10% body weight.[7] Clinical practice guidelines currently recommend a weight loss of at least 7% to 10% to achieve histologic improvement in steatohepatitis and necroinflammation.[1]

Exercise and Physical Activity

Physical activity is one of the best methods to achieve weight loss. By itself, exercise is an effective method of decreasing hepatic steatosis, even in the absence of body weight loss.[8–10] Metabolic profiles of patients improve, decreasing overall cardiovascular disease risk. Both aerobic exercise and resistance training are effective. A positive effect on hepatic steatosis, as demonstrated by MRI, can be seen with only 8 weeks of strength training.[11] At least 60 minutes of aerobic exercise shows benefit, but longer durations, up to 150 minutes per week, were optimal. Studies of exercise and its effects on NAFLD are limited by small samples sizes. Given the low cost of exercise and the health risks of increasingly sedentary lifestyles, however, physical activity and weight loss should be one of the first interventions in the treatment of NAFLD.

Dieting and Nutrition

Compared with healthy individuals, those with NAFLD consume a diet higher in certain fats and cholesterol, excessive in calories and fructose, while lacking in vitamins and fiber.[12] The type of dietary fats that are associated with NASH are saturated fats and cholesterols.[13–15] Clear evidence for a direct causal relationship, however, between these macronutrients and NAFLD/NASH, in humans, is lacking. Trans–fatty acids and monounsaturated fatty acids have been studied only in animal models; thus, their association with NAFLD in humans is not proven.[16–18] Other fats, namely omega-3 fatty acids or n-3 polyunsaturated fatty acids (PUFAs) might be protective.[19,20] Randomized trials with histologic improvement as an endpoint have not shown significant improvement in NAS,[21,22] and PUFA supplementation is not currently recommended as treatment of established NAFLD. Given the increased consumption of processed