

NASH IN FOCUS

Current Developments in the Management of Nonalcoholic Steatohepatitis

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Lifestyle Modifications for Patients With Nonalcoholic Steatohepatitis



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G&H What is the role of diet and exercise in the treatment of patients with nonalcoholic steatohepatitis?

SZ-S Nonalcoholic steatohepatitis (NASH) is mainly a lifestyle-oriented disease, so it is not surprising that the cornerstone of treatment is lifestyle modification. There are also other causes of NASH, such as genetics, but lifestyle is the main cause for NASH and, therefore, is the main route of treatment and also prevention. Lifestyle modifications involving diet and physical activity can be effective in every stage of nonalcoholic fatty liver disease (NAFLD), including NASH with and without fibrosis, and can reverse advanced stages of fibrosis up to cirrhosis. Cirrhosis is typically not reversible with diet, although diet can help treat it and prevent hepatocellular carcinoma.

G&H Which dietary components should be avoided and which should be recommended in patients with NASH?

SZ-S Several dietary factors are strongly related to NAFLD and NASH. One is sugar, specifically fructose. Both of these are lipogenic and are related to increased amounts of liver fat, NASH, and fibrosis. These findings have even been demonstrated among children. Especially harmful is sugar from sugar-sweetened beverages, which contain high amounts of sugar that are absorbed quickly. Many studies have been conducted on sugar-sweetened beverages in both children and adults.

Another nutritional factor is saturated fat. Many randomized clinical trials have shown that overconsumption

of saturated fat, as compared with unsaturated fat, leads to an increased amount of liver fat. Therefore, foods that are rich in saturated fat, such as high-fat meat, cheese, butter, and sweets, are not recommended in patients with NASH. Ultra-processed foods, which contain a large amount of both saturated fat and sugar, are likewise not recommended in patients with NASH. Other foods to avoid include red and processed meats, which are associated with NAFLD.

The polar opposite of an ultra-processed or fast food diet is the Mediterranean diet, which is mostly based on natural and fresh foods, home-based cooking, fruits, vegetables, legumes, whole grains, fish, and white meat. That may explain why the Mediterranean diet has been demonstrated in several large randomized clinical trials to be a good treatment for patients with NAFLD, reducing the amount of liver steatosis. However, the exact effect of this diet on NASH is not known because those studies did not obtain repeat liver biopsies.

It is also important to note that patients do not need to follow a very strict, radical diet. They may feel that they cannot eat any foods because no foods are healthy enough. In reality, there are many foods that can be eaten; the Mediterranean diet, for example, includes many appetizing foods. It is most important to reduce sugar and ultra-processed food, although it is not necessary to completely eliminate them. Patients can make reasonable dietary modifications and still have a healthy diet that is sufficient to improve the health of their liver.

G&H Can vitamins play a role in the treatment of patients with NASH?

SZ-S Vitamin E and vitamin C have been inversely related to NAFLD and NASH in observational studies. Large clinical trials have also shown that vitamin E has a beneficial effect in patients with NASH. The more fruits and vegetables in a diet, the more vitamins there are, which is part of the reason the Mediterranean diet is beneficial in patients with NASH. Also beneficial are polyphenols. In a large randomized trial, following the Mediterranean diet enriched with polyphenols resulted in even better reduction of liver fat than the Mediterranean diet without polyphenols. Even without such enrichment, the Mediterranean diet itself is rich in polyphenols found in vegetables, nuts, and especially olive oil.

G&H What amount, type, and duration of exercise should be recommended for patients with NASH?

SZ-S Most studies have looked at 2 to 3 exercise sessions per week of 40 to 45 minutes each of moderate aerobic exercise or resistance exercise. Both types of exercise appear to have similar effects on liver fat reduction. These are very good results that are beneficial even if weight reduction does not occur. These results show reduction of liver fat, but the effect of exercise on the more advanced, inflammatory form of NAFLD—NASH—has not been examined because of a lack of liver biopsy in these studies.

Several studies have looked noninvasively at fibrosis and found that exercise produced a probable beneficial effect on fibrosis reduction. One clinical trial with a very small sample size obtained repeat liver biopsies and found an improvement in liver fibrosis in some of the patients after 12 weeks of aerobic exercise. This finding is very encouraging, but more evidence is needed.

G&H Are modifications of both diet and exercise needed, or is dietary modification typically sufficient for the treatment of patients with NASH?

SZ-S Usually, modifications of both diet and exercise are needed for long-term results. This can be difficult for patients, but they can start with just their diet and make small steps in dietary modifications first. However, eventually providers need to explain to patients that even small or moderate changes in physical activity can be very helpful. For example, even increasing the amount of time walking or even doing yoga or resistance training once or twice a week can be beneficial. Patients do not necessarily need to exercise very intensively, as even small changes can make a big difference.

Physical activity is also important for the prevention of cardiovascular disease, hepatocellular carcinoma, and

type 2 diabetes, which are all increased in patients with NASH. Physical activity has also been shown to be critical to maintaining weight reduction.

G&H Are any other lifestyle modifications (eg, involving alcohol, smoking, coffee, and sleep) beneficial in patients with NASH?

SZ-S The effect of alcohol has been debated. Earlier studies have suggested that low alcohol consumption, defined as 1 serving per day or less, is not harmful in NAFLD and may even have some beneficial effects. However, importantly, good prospective studies in recent years have shown that even very modest alcohol consumption can lead to liver fat accumulation, less resolution of NASH, greater progression of fibrosis, and greater risk of hepatocellular carcinoma. Therefore, most guidelines now recommend avoiding alcohol consumption as much as possible. If patients insist on consuming alcohol, the limit should be 1 glass of wine per day, but only for patients without fibrosis. Patients who have significant or advanced fibrosis should not drink at all because alcohol increases the risk of hepatocellular carcinoma. Likewise, smoking is related to hepatocellular carcinoma as well as fibrosis, and should thus be avoided.

In contrast, coffee has been related to the prevention of hepatocellular carcinoma in large epidemiologic studies. Therefore, patients are welcome to drink a reasonable amount (3-5 cups usually) of coffee per day, and any type of coffee can be beneficial.

As for sleep, research findings have been conflicting. It is difficult to conclude whether sleep is directly related to NAFLD, as some studies suggest that it is, whereas others suggest that it is not. Regardless, good sleep is important in general and specifically for the prevention of obesity and unhealthy eating. Sleeping approximately 7 hours per night is recommended.

G&H What strategies can be used to help facilitate long-term maintenance of lifestyle modifications and to avoid relapse?

SZ-S It is well known that long-term adherence to lifestyle modifications is important. To achieve this goal, patients should have a good understanding of the disease and that it is reversible with diet and exercise, and providers should help motivate patients. Patients also need to understand that relapse is normal, occurs frequently, and is not disastrous. Relapse is part of the process, and patients just need to start over again.

It is also important to set realistic goals with patients. If they want to reduce 20% of their initial body weight, providers should explain that such a large goal may be

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difficult to achieve and maintain in the long term, and may not be entirely necessary. Weight reduction of 5% to 10% is typically sufficient to treat steatosis and NASH, and treating fibrosis may necessitate a weight reduction of 7% to 10%. These are realistic goals.

In addition, it is important to tailor the modifications to individual patients. Some patients prefer low-fat diets, others prefer low-carbohydrate diets, and others prefer intermittent fasting. Providers should ask their patients what they like to eat and what they are willing to give up eating to tailor the diet personally to each patient.

Providers should also explain that dietary modification is a lifelong treatment. Patients can see a dietitian less frequently after the start of treatment but will need to stay in constant contact with a dietitian to maintain weight reduction.

G&H What treatment options other than lifestyle modifications are currently available for patients with NASH?

SZ-S Medical treatment is not currently available specifically for the treatment of patients with NASH. When diet and exercise fail repeatedly, weight reduction can be attempted with medications or, for patients with morbid obesity, bariatric surgery. As discussed, weight reduction can be beneficial for treating NASH. Regardless of the subsequent therapy, lifestyle modifications should always be part of the treatment for NASH.

G&H Do you have any advice for physicians involving the management of NASH with lifestyle modifications?

SZ-S Physicians play a crucial role in creating motivation for their patients' lifestyle modifications. Although physicians have a short time with patients, it is important to ask how they are doing with their diet. Physicians should also remind patients that NASH is a reversible disease that can be treated with a healthy diet. Giving patients a small tip at each visit can be helpful. For example, physicians

can encourage patients to start by stopping soft drinks at one visit. Then physicians can follow up the next visit to see how that change is going and whether patients can progress to the next step. Physicians should refer patients to nutritional treatment programs, as structured lifestyle intervention can be highly beneficial.

G&H What are the priorities of research in this area?

SZ-S We need large randomized clinical trials of diet and physical activity in patients with NASH not only looking at liver fat reduction, but also at an outcome of NASH resolution by liver histology and fibrosis regression using noninvasive methods as much as possible. Better noninvasive assessments are needed because it is difficult to perform large studies with repeat liver biopsies. In addition, we need to perform large long-term trials to look at clinical outcomes to determine whether dietary intervention prevents cirrhosis, severe liver events, and hepatocellular carcinoma.

Disclosures

Dr Zelber-Sagi has no relevant conflicts of interest to disclose.

Suggested Reading

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