

An Exploration of the Treatment of Non-Alcoholic Fatty Liver Disease Based on Dietary Factors

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Abstract. Non-alcoholic fatty liver disease is a clinical pathological syndrome characterized by diffuse hepatocellular macrovesicular steatosis caused by other liver-damaging factors except for alcohol. At present, there are no specific drugs for non-alcoholic fatty liver disease in the Eastern world or the Western world, so dietary factors play an important role in the prevention and treatment of non-alcoholic fatty liver disease. In this review, we briefly discussed the roles and mechanisms of dietary components (including fructose, protein, and vitamins) in the progression or prevention of non-alcoholic fatty liver disease. Although patients with non-alcoholic fatty liver disease can benefit from weight loss, excessive reduction of food intake can exacerbate fat accumulation in hepatocytes. In addition, we discussed the Mediterranean dietary pattern and compared the effectiveness of low-fat and low-carbohydrate diets in preventing the development of non-alcoholic fatty liver disease.

1 Research Background and Significance

Non-alcoholic fatty liver disease is a clinical pathological syndrome characterized by diffuse hepatocellular macrovesicular steatosis caused by other liver-damaging factors except for alcohol [1], and its incidence rate has been increasing [2], becoming the first chronic liver disease in the world [3].

In recent years, the prevalence of non-alcoholic fatty liver disease is as high as 25% in China, which has surpassed some developed countries in Europe and the United States and become the first major chronic liver disease in China. It has involved 1/3 of the population globally and become an important cause of liver disease related complications and death [4], and is the primary cause of abnormal liver biochemical indices in a health examination. The most important risk factors for this disease are obesity and metabolic syndrome. Non-alcoholic fatty liver disease is a clinically common chronic liver disease, which is not only common in adults, but also has a high prevalence in children and adolescents. With the continuous development of modern society, the increasing abundance of material and nutrition, the change of people's living habits and working style, the youth and some office workers who lack exercise for a long time have also become the high incidence of this disease, which has gradually attracted people's attention. Therefore, how to effectively reduce the incidence of non-alcoholic fatty liver disease and restore liver function is the focus and difficulty of the treatment of this disease, and how to explore a safe and efficient treatment method that can be accepted by the

patients and recognized by the majority of medical personnel is the focus of our attention.

2 Analysis of Domestic and International Research Status

In the Western world, hepatic steatosis first originated in 1842 as a pathologic change when the British anatomist William Bowman published a report entitled "The minute anatomy of fatty degeneration of the liver" in the *Lancet* after observing the specimen of human liver under a microscope. In the following century, it was still widely believed that the cause of fatty liver was chronic heavy alcohol consumption. It was not until around 1980 that, on the basis of previous studies, Ludwig, a researcher at the Mayo Clinic, first proposed non-alcoholic pancreatitis and Schrieffer proposed the concept of non-alcoholic fatty liver disease (NAFLD), formally establishing NAFLD as a disease.

In ancient China, there was no name for NAFLD in ancient Chinese medical literature, but there were records and treatments for symptoms similar to those of NAFLD. From the perspective of Chinese medicine, NAFLD is also known as "liver amassment disease" and "hypochondriac pain". For example, the *Classic on Medical Problems* says, "The fats accumulation of liver is called liver amassment", and the *Miraculous Pivot. Five Pathogens* says, "If the pathogen attacks the liver, there will be hypochondriac pain".

From the perspective of Chinese medicine etiology and pathogenesis of NAFLD, the physician Chao Yuanfang in the Sui Dynasty pointed out in the *General Treatise on the Cause and Symptoms of Diseases* that

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"the disease is caused by the improper temperature, resulting in the weakness of the internal organs, the food is not digested and agglomerated inside, and gradually growing into a block, which does not move. It can be verified by describing its shape. If the accumulation continues for many years, the person will become thin, but his abdomen will become big, and then he will die." This suggests that improper diet is an important pathogenic factor in NAFLD.

Nowadays, the main methods of Western medicine to treat NAFLD are as follows: 1. Changing bad lifestyle. That is, by restricting dietary intake and combining appropriate exercise, strengthen the patient's cardiopulmonary function, reduce the risk of cardiovascular disease, and effectively alleviate or even reverse NAFLD; 2. Drug therapy. Among them, the role of drug therapy has two main directions: (1) Drug therapy for liver injury, mainly focusing on restoring liver function; (2) Drug therapy to promote hepatic lipid metabolism. At present, insulin sensitizers, antioxidants, hepatocyte protectants and other agents are commonly used in Western medicine for the treatment of NAFLD, but there is a lack of unified special drugs [5].

Chinese medicine treatment emphasizes on the treatment based on syndrome differentiation, eating disorders and overeating fat, sweet and heavy flavors are important causes of NAFLD. Li Dongyuan's Treatise on the Spleen and Stomach says, "Fat and heavy flavors breed sputum." It points out that if the diet is not proper, the food cannot be transported and digested, forming sputum, which damages the spleen and stomach over time, thus making the stagnation of qi movement, and the retention of water and dampness, resulting in qi, blood, sputum and turbidity gathering with each other and being accumulated in the liver, and thus triggering this disease. Therefore, Chinese medicine practitioners often use traditional Chinese medicine prescription for treatment, such as in the mild fatty liver stage, with liver depression and spleen deficiency and syndrome of accumulated dampness-heat, phlegm and stasis and other pathological factors have not yet been formed, with the chief prescription of Xiaoyao Powder, Sanren Decoction and Yinchen Wuling Powder; in the middle fatty liver stage, with dampness and turbidity stasis, and deficiency of the spleen and kidney, with the use of Weiling Decoction and Sijunzi Decoction and Jingui Shenqi Pill; in the severe fatty liver stage, with phlegm and stasis syndrome, using Infradiaphragmatic Stasis-Expelling Decoction and Erchen Decoction [6]. In addition, clinical studies have shown that the efficacy of external Chinese medical treatments such as acupuncture, manipulation, application, auricular point and cupping in NAFLD is obvious, which can significantly reduce the patient's blood lipid level, improve liver function, and even reduce weight, thus effectively relieving clinical symptoms [7]. However, Chinese medicine still lacks the identification of constitutional pattern, and the clinical patterns have not been standardized. From the perspective of etiology and pathogenesis, traditional Chinese medicine practitioners also believe that improving dietary structure can be a good treatment for NAFLD.

In conclusion, both Western and Chinese medicine believe that improper diet is an important reason for the development of NAFLD, and both require patients to control their diets and exercise appropriately.

At present, dietary modification for the treatment and control of NAFLD has received widespread attention as a low-risk and low-cost strategy for patients with NAFLD. Studies have shown that poor dietary habits, such as high calorie, excessive sugar and fat intake, are important factors in the development of NAFLD [8].

3 Dietary Components and Types

Table 1. Dietary Types and Components That Promote or Ameliorate NAFLD

| | Promote NAFLD | Ameliorate NAFLD |
|------------------------|---------------|------------------|
| Red meat | Yes | No |
| Saturated fatty acid | Yes | No |
| Unsaturated fatty acid | No | Yes |
| Protein | No | Yes |
| Fructose | Yes | No |
| Ethanol | Yes | No |
| Vitamin | No | Yes |

3.1 Red meat consumption promotes fatty liver

Red meat refers to the muscles, organs and products of livestock including pigs, cows and sheep. The muscles of red meat are dark red in color and deep in texture, that's why it's called red meat. From a nutritional perspective, red meat has a high-fat content and is rich in unsaturated fatty acids. Recently, a growing number of studies have shown a positive correlation between red meat intake and the likelihood of NAFLD [9]. Therefore, it is necessary for patients with NAFLD to limit red meat intake (table 1).

3.2 Excessive intake of fructose increases the risk of fatty liver disease

Fructose is a monosaccharide. It occurs naturally in fruits honey and some vegetables and is the main ingredient in the two most commonly used sweeteners, sucrose and high fructose corn syrup [10]. Fructose is metabolized primarily in the liver. A small amount of fructose is converted to glucose by the small intestine, and most fructose, especially when consumed in liquid form, can be absorbed directly and enter the liver through the portal vein, increasing liver stress and enhancing the risk of NAFLD. Some studies have pointed out that the fructose molecule itself is not primarily responsible for the production of triglycerides, but rather for the accumulation of fat in the liver by activating lipogenesis and blocking fatty acid oxidation. Research on fructose and NAFLD continues, but it is clear that reducing fructose intake has benefits for patients with NAFLD.

3.3 Moderate intake of protein is beneficial to patients with fatty liver

Consuming a protein diet in large quantities has some side effects on the body, but moderately increasing the proportion of protein in the daily diet can be beneficial for patients with NAFLD. In a rat model, a high-protein diet was reported to reduce hepatic lipid accumulation compared with a normal protein diet, and the reduction was greater when combined with restricted calorie. A randomized controlled trial by Markova et al. showed that two isocaloric diets rich in either animal or plant proteins (30% protein, 40% carbohydrates, and 30% fat) reduced intrahepatic lipids by 36%-48% in individuals with type 1 diabetes. It can be seen that the hepatic fat metabolism of protein has an auxiliary role. In addition, an increase in the proportion of protein in the diet usually leads to a decrease in carbohydrate intake. For patients with NAFLD, protein in food produces a greater sense of satiety than carbohydrates and fats, thus contributing to weight loss.

3.4 Ethanol intake is harmful to fatty liver

Ethanol is an organic substance, commonly known as alcohol, which is the main ingredient of wine. As a worldwide drink, alcohol has always been loved by people. Although it has a distinctive flavor and can be pleasurable, it has also brought harm to humans. NAFLD is considered to be the counterpart of alcohol-related liver disease, as it is defined as hepatic steatosis without excessive alcohol consumption. However, there is still controversy about whether alcohol consumption has an effect on the subsequent development of NAFLD. Some studies have shown that there is a beneficial aspect of moderate alcohol consumption on the development and progression of NAFLD. However, Ajmera et al. showed that moderate alcohol consumption was associated with less improvement in steatosis and aspartate aminotransferase levels and lower odds of non-alcoholic steatohepatitis remission compared to non-drinkers. Over the past few years, there has been increasing evidence that alcohol has considerable harmful effects, with recent guidelines recommending complete abstinence from drinking. Moderate alcohol consumption in patients with NAFLD has multiple effects and conflicting results have been reported. Therefore, based on the basic medical principle of "no harm", it is recommended that patients with NAFLD, especially those with co-morbidities or advanced hepatic fibrosis, should reduce or even refuse alcohol intake.

3.5 Supplementing vitamins can improve fatty liver

Vitamins are a class of trace organic substances that must be obtained from food to maintain normal physiological functions in humans and animals, and play an indispensable role in human growth, metabolism, and development. Nowadays, although studies have shown that vitamin D deficiency is common in patients with

NAFLD, the relationship between vitamin D and NAFLD has yet to be studied. In addition, vitamin D supplementation has been shown to improve insulin resistance and serum liver enzyme levels, making it beneficial for patients with NAFLD.

4 Mediterranean Diet

Excessive accumulation of visceral fat may lead to the production of a variety of adipokines and hormones, which may contribute to lipolysis, resulting in the production of free fatty acids and their deposition in the liver, exacerbating NAFLD. Therefore, patients with NAFLD may benefit from weight loss and obesity control. However, in terms of the speed and extent of weight loss, it has been found that when patients with NAFLD lose weight too rapidly by controlling their caloric intake, it may exacerbate the accumulation of fat in the hepatocytes and lead to further development of inflammatory reactions and fibrosis in the portal veins. Moreover, prolonged reduction of food intake can lead to decreased compliance. Therefore, choosing a dietary pattern that helps to control NAFLD lesions without making people feel very hungry is an urgent consideration.

The Mediterranean diet is a nutritional pattern that originated in the countries surrounding the Mediterranean Sea. While the Mediterranean dietary pattern may vary from country to country and region to region owing to cultural, ethnic, religious and agricultural differences, a common Mediterranean dietary pattern includes a predominant consumption of unrefined grains, vegetables and fresh fruits, olive oil and nuts; a moderate consumption of fish, white meats and legumes; a restriction of red and processed meats and sweets; and a moderate consumption of red wine (table 2).

Table 2. Food Types and Nutritional Factors in the Mediterranean Diet

| Types | Nutritional Factors |
|-------------------|---|
| Fresh fruit | Vitamin C, polyphenols, carotenoids and fiber |
| Vegetable | Vitamin C, polyphenols, ω -3-PUFA, carotenoids and fiber |
| Olive oil | MUFA and polyphenols |
| Coarse food grain | Polyphenols and fiber |
| Nuts | Polyphenols, ω -3-PUFA and fiber |
| Beans | Polyphenols and fiber |
| Fish | ω -3-PUFA |
| Wine | Polyphenols |

Inflammation and oxidative stress are important responses to NAFLD, and components of the Mediterranean diet have anti-inflammatory or antioxidant effects. Flavonoids are polyphenolic compounds commonly found in vegetables and fruits that have antioxidant, anti-inflammatory and hepatoprotective properties. In addition, carotenoids are natural fat-soluble pigments that act as antioxidants in the Mediterranean diet.

The beneficial effects of the Mediterranean diet on hepatic lipid metabolism are mainly influenced by its fatty acid composition, which is high in unsaturated fatty acids, with the main food components being vegetables, legumes, nuts, olive oil and fish (not red meat). And, several studies have shown that reduced saturated fat intake is associated with lower plasma concentrations of total cholesterol, very low-density lipoprotein (LDL) cholesterol, and triglycerides.

Therefore, the Mediterranean diet not only helps to improve oxidative and inflammatory responses in NAFLD but also lowers lipids and promotes liver metabolism.

Cara B. Ebbeling et al. demonstrated the effects of an isocaloric low-fat diet, a low-glycemic diet, and a low-carbohydrate diet on the maintenance of weight loss in overweight or obese young adults on three different components of an isocaloric diet, which resulted in 10% to 15% weight loss during the initial phase, accompanied by reductions in resting energy expenditure and the thermic effect of exercise, with the low-carbohydrate group having the least decrease in resting metabolic rate and the most effective in maintaining energy expenditure. It can be seen that the low-carbohydrate diet is a cost-effective dietary pattern.

5 Conclusion

In conclusion, the treatment of NAFLD by dietary modification is characterized by low risk and high benefit, with the Mediterranean diet being a good dietary pattern that can be recommended to patients.

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