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Research Progress of Chinese and Western Medicine in the Treatment of Non-Alcoholic Fatty Liver Disease

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Abstract: NAFLD has been the most common cause of chronic liver disease, with a global prevalence of NAFLD of approximately 34.2% in the total population. Children currently have limited treatment options for NAFLD, which mainly include non-pharmacologic, pharmacologic and surgical treatments. Currently, Western medicine is mainly based on symptomatic management with lipid-lowering drugs, insulin-sensitizing drugs, and drugs to regulate intestinal flora and immune function. Chinese medicine is based on the diagnosis of Chinese medicine, and the treatment of liver and spleen, removing dampness and turbidity, clearing heat and dampness, activating blood circulation and removing blood stasis, which has a better clinical effect, and the treatment of traditional Chinese medicine can help to improve the efficacy of western drugs, alleviate the toxicity of liver and kidney of western drugs, and improve the overall resistance of the patient to slow down the development of the disease, therefore, the way of traditional Chinese medicine and the combined use of traditional Chinese medicine can be used as a direction of the research in the future, and the way of traditional Chinese medicine in the treatment of nonalcoholic fatty liver disease has a bright future. Therefore, the combined application of TCM and TCM gongfu can be the direction of future research.

1. Introduction

Nonalcoholic fatty liver disease (NAFLD), also known as metabolic associated fatty liver disease (MAFLD), is defined as the presence of steatosis in >5% of hepatocytes in the absence of recent or previous heavy alcohol consumption and other liver diseases. Steatosis is present in >5% of hepatocytes in the absence of recent or previous heavy alcohol consumption and other liver diseases. NAFLD has been the most common cause of chronic liver disease, with a global prevalence of NAFLD of approximately 34.2% in the total population[1].Patients with NAFLD can progress from simple fatty liver to nonalcoholic steatohepatitis (NASH). Current treatment options for NAFLD are limited and consist of nonpharmacologic, pharmacologic, and surgical treatments. Non-pharmacologic treatments are mainly lifestyle interventions and weight loss, and pharmacologic treatments are mainly lipid-lowering drugs and symptomatic drug therapy. At present, the clinical treatment of western medicine for the prevention and treatment of NAFLD is more mature, mainly

for changing lifestyle habits, exercise therapy and symptomatic treatment. Clinical practice and experience have shown that traditional Chinese medicine has better efficacy in slowing down the progression of the disease and regulating blood indexes and improving clinical symptoms.

2. Etiological analysis

The cause of NAFLD is still unclear, and there are several causes of NAFLD that are currently recognized by most people.

(1) Obesity: Obesity is an abnormal state of lipid metabolism that leads to the accumulation of fat in the body. Obesity is a common cause of chronic liver disease in children with NAFLD. Some studies have found[2]. The prevalence of NAFLD in overweight/obese children is 38.2%. Because obesity is prone to insulin resistance, increased FFA and abnormal expression of various cytokines, it may increase the risk of NAFLD.[3].

(2) Insulin resistance, IR: Some studies have found[4],Binding of insulin to the insulin receptor promotes phosphorylation of the substrate. When the sensitivity of the effector organs of insulin action to insulin is reduced, there will be a compensatory increase in insulin, which will eventually develop into hyperinsulinemia. Once the compensatory increase in insulin secretion occurs, it can promote the hepatic synthesis of total cholesterol (total cholesterol (TC)), and also elevate the low-density lipoprotein (LDL), which will lead to the inactivation of lipoprotein lipase and decrease the removal of TG, which will eventually induce the development of NAFLD. A large amount of TG accumulates in the liver, which ultimately induces the development of NAFLD.

(3)Imbalance of intestinal flora: Gut microorganisms change their phenotype and virulence from symbiotic mode to pathogenic mode by sensing various adverse signals generated by intestinal stress, resulting in damage to the organism. Numerous studies have found that gut microbial disorders are closely related to the development of NAFLD.[5].

(4) Genetic factors: The risk of NASH has been found to be influenced by polymorphisms in single nucleotide genes. Patatin like phospholipase domain containing protein 3 (PNPLA3) is one of the members of the patatin-like phospholipase family that has been found to be closely associated with the development of NAFLD in recent years. Patatin-like phospholipase domain 3 (PNPLA3) is a member of the patatin-like phospholipase family[6].

(5) Imbalance in intrinsic immune regulation: the development of NAFLD is often accompanied by an imbalance in the intrinsic immune system. It has been found that the main feature of NAFLD is the presence of a large population of intrinsic versus infiltrating immune cells. Clinical etiology is complex and varied, mostly due to multiple etiologic factors[7].

3. Mechanism studies

3.1 Western medical mechanism

The pathogenesis of NAFLD is complex and not yet well understood[8]. Some studies believe that obesity is the main factor causing NAFLD. Obese people have excessive adipose tissue content, which increases the rate of lipolysis and metabolism, thus increasing the content of free fatty acids (FFA) in the organism. Free fatty acids will enter the liver with the flow of blood, leading to the formation of fatty liver. Obese individuals have an increased risk of developing IR. Increased blood insulin concentration in IR patients leads to glucagon inhibiting the release of lipoproteins from the liver, which causes triacylglycerol deposition in the liver, resulting in the formation of NAFLD. Intestinal flora, mononucleotide genes, phagocytosis, and T-cell activation have an impact on the progression of NAFLD.

3.2 Chinese medicine etiology and pathogenesis

Chinese medicine can be attributed to the category of "liver fetish", "dystocia", "accumulation". Mostly due to dietary disorders, labor and leisure, emotional disorders, chronic illness, physical weakness, and endowment deficiency, these factors result in liver loss of drainage, spleen loss of healthy transport, phlegm, dampness and stasis of each other, congestion of the liver, the body's fat, and turbid qi excessive accumulation in the liver, which are the main manifestations of the disease leading to coercive and rib distension and pain.

The mechanism of this disease is spleen deficiency and dysfunction. Spleen is "the foundation of the latter day", the main transportation, transmission and distribution of water and grain essence, as the source of qi and blood biochemistry. "When the spleen is deficient, it is unable to transport and regulate properly, which results in the accumulation of evils in the middle jiao and the development of the disease. Phlegm-drinking, dampness-heat and blood stasis are the main pathological factors, and the normal operation of the spleen and stomach is the basis for the production, transportation and transmission of water and grain essence in the human body. In the early stage of the disease, when the spleen is deficient in transportation, the transmission and distribution of essence is abnormal, which turns into water-dampness and phlegm-drink. As the disease progresses, the turbid evil stops gathering in the middle jiao for a long time, and becomes hot, and there is dampness and heat inside, and the disease mechanism changes from deficiency to reality, and the deficiency and reality are mixed. Innate endowment insufficiency, or long-term disease and kidney, kidney essence deficiency, the disease mechanism from solid to virtual, qi and transformation failure, phlegm and turbid not transformed, the internal knot blockage of qi, qi stagnation and blood stasis, blood stasis and blockage, phlegm and stagnation of each other.

4. Treatment

4.1 Western medicine

NAFLD belongs to the metabolic disease, at present the mild disease in the treatment is mainly in the weight loss on the basis of giving symptomatic treatment. Clinical drugs used in western medicine mainly include the following categories:①Lipid-lowering drugs: At present, the best lipid-lowering effect of drugs for statins, its mechanism is mainly through the inhibition of HMG-CoA reductase activity, to prevent the conversion of HMG-CoA to 2-methylpentanoic acid, reduce the synthesis of endogenous cholesterol, and increase the number of LDL-C receptors on the surface of hepatocytes, so that the hepatocytes of the uptake and metabolism of LDL-C ability to enhance the reduction of free fatty acid accumulation in cytoplasm, to control NAFLD from the source. Fatty acid accumulation, from the source to control NAFLD. At the same time, statins can also play an antioxidant and anti-inflammatory effect[9].②Insulin sensitizers: Patients with IR need to take insulin sensitizers to enhance the sensitivity of effector organs to insulin. At present, insulin sensitizers commonly used in clinical practice mainly include: metformin, thiazolidinediones and so on. Metformin can reduce the production of mitochondrial reactive oxygen species and normalize oxidative metabolic markers. Long-term use of metformin can not only directly alleviate the chronic oxidative stress induced by high-fat diets in liver tissues, but also effectively protect the liver from acute oxidative damage.③Regulate intestinal flora and immune function drugs: some studies have found that prebiotics can reduce fat production, reduce the expression of fatty acid synthase (FAS) and other genes, and ultimately reduce the accumulation of TG in the liver[10].Total saponins of Gynostemma gibberelliforme can significantly reduce the ratio of Bacillus thickeniensis to Bacillus anthropophilus in high-fat diet-fed rats, significantly increase the abundance of beneficial bacterial

flora such as Ackermannella spp, Lactobacillus spp, and Micrococcus wartii, reduce the relative abundance of harmful bacterial flora, restore the diversity of intestinal flora, and reduce the hepatic inflammatory response to achieve the effect of anti-NAFLD[11].If severe fatty liver disease eventually leads to cirrhosis and liver failure, liver transplantation is needed. At present, the clinical western medicine treatment is commonly used to change the lifestyle habits and lipid-lowering drug treatment, clinical commonly used lipid-lowering drugs or atorvastatin calcium, insulin sensitizing drugs, regulating intestinal flora drugs for the treatment of complications.

4.2 Chinese medicine

4.2.1 Chinese medicine prescription

According to the different causes and symptoms, Chinese medicine practitioners classify NAFLD into four types: Liver Depression and Spleen Deficiency, Dampness and Turbidity, Dampness-Heat Conjugation and Phlegm-Stasis Conjugation. The main ideas of Chinese medicine treatment are: dredging the liver and strengthening the spleen, eliminating dampness and resolving turbidity, clearing heat and resolving dampness, activating blood circulation and removing blood stasis. Some famous doctors use different prescriptions to treat the disease with their own experience. According research[12], Prof. Zhang Lei used Reed Stem Soup as the main formula for NAFLD with phlegm and stagnation, and for obese patients with fatty liver who are addicted to fat, sweet and thick flavors, fat and sleepy, with white and greasy tongue, and whose evidence belongs to phlegm-dampness obstruction, Er Chen Soup can be used together to dry up the dampness and resolve the phlegm. According to Li Heguo's research[13],Prof. Li Zhenhua, a master of Chinese medicine, takes strengthening the spleen and transporting dampness as the basic principle of treatment for this disease, and at the same time combines the methods of regulating qi and eliminating dampness with detoxifying the liver and activating the blood, so as to make the qi and blood flow smoothly, and the wood does not multiply by the earth, so that the spleen and qi are able to move healthily and to determine the source of phlegm. Strengthening the spleen and transporting dampness is the basic principle of treatment for this disease, and at the same time, the method of regulating qi and eliminating dampness, dredging the liver and activating the blood should be used, so as to make the qi and blood flow smoothly, the wood does not multiply by the earth, and the spleen qi is healthy to transport, so as to determine the source of phlegm production. According to Yuan Yuan Tsai's research[14],Prof. Ling divided the disease into three stages; early liver depression and spleen deficiency corresponds to the prescription for the self-designed slow moving liver formula, the composition of drugs including Chai Hu, Angelica sinensis, white peony, Radix Paeoniae Alba, Radix et Rhizoma Atractylodis Macrocephalae, Poria cocos, Salviae Miltiorrhizae, Shenquan, licorice, etc.; In the middle of the phlegm-dampness internal stagnation, which corresponds to the prescription for Ping Gastric San combined with the slow moving liver formula, if it is a dampness-heat condensation syndrome, then the corresponding drugs to choose are those that clear the heat and promote dampness, such as Insecticidia sinensis, Rheum Palmatum, Gardenia jasminoides, chicken bone grass, etc.; in the late stage of the disease, the drugs include Angelica sinensis, Salvia miltiorrhiza, Uljin, Dampy, Astragalus, Rhizoma Atractylodis Macrocephalae, and so on.

Famous experts have not yet formed a consistent theory, mainly based on the clinical efficacy of the main.

4.2.2 Modern Pharmacology

Modern medical research on single-flavored drugs for the treatment of this disease has also seen

new developments; ① Berberine is an important active ingredient in Huanglian, whose main effect is anti-inflammatory and analgesic, and it is a commonly used drug in Chinese medicine clinics.Some studies have shown that[15],Berberine can improve hepatic fat deposition induced by high-fat diet, reduce the expression of hepatic inflammatory factors IL-6 and TNF-α to improve hepatic inflammation; and promote the polarization of hepatic macrophages to M2 type to improve hepatic inflammation and repair damaged tissues. Meanwhile, berberine can also increase the activity of mitochondrial superoxide dismutase (Mn-SOD) to reduce the generation of mitochondrial reactive oxygen species (mtROS) to reduce the damage of hepatocytes and regulate the activation of hepatic macrophages.②Huperzia is a traditional Chinese medicine in China, which has a good effect on liver diseases, while and Huperzinol is the main component of the Chinese medicine Huperzia, which has a variety of effects such as antioxidant, anti-inflammatory, lipid-lowering, anti-tumor and so on.Some studies have shown that[16], which can activate the PPARα/ACOX1/CPT1A signaling pathway, which in turn promotes fatty acid β-oxidation, attenuates lipid deposition, and reduces oxidative stress and inflammatory response. Pueraria Mirifica is one of the pungent, cool and antidiarrheal herbs in traditional Chinese medicine, which has the efficacy of elevating yang, reducing fever, generating body fluid, detoxifying muscles, promoting collaterals and stopping diarrhea.③Puerarin is the active ingredient extracted from Pueraria Mirifica, which has obvious therapeutic effects on lipid metabolism, glucose metabolism and insulin resistance. It has been found that Pue, the active ingredient of Puerarin, can trigger autophagy through the PI3K/Akt/mTOR pathway, thereby reducing fat deposition and inflammation. Puerarin also induced the expression of adipose triglyc-eride lipase (ATGL) in the liver, which enhanced the activity of 5´AMP-activated protein kinase (AMPK), which is a central regulator of hepatic lipid metabolism. The activation of AMPK, a central regulator of hepatic lipid metabolism, may be mediated by SIRT1 and the calcium signaling pathway involved in G protein coupled estrogen receptor (GPER) signaling, and thus Puerarin may improve steatosis in NAFLD by activating GPER.

4.2.3 External treatment with Chinese medicine (TCM)

External treatments in Chinese medicine, which also play an important role in complementary medicine and herbal therapy. Some studies have shown that[17],The treatment in acupuncture combined with degree patch can effectively reduce inflammatory factors, accelerate blood circulation, promote lipid metabolism, and improve liver function without the toxic side effects of drugs. Some studies have shown that[18],Chinese medicine gymnastics eight-duanjin can improve the vagus nerve excitability, enhance fat metabolism, regulate the state of blood lipid distribution, etc., effectively improve the symptoms of non-alcoholic fatty liver. Acupuncture Point Embedding, a specialized therapy in Chinese medicine, has available clinical data for analysis. This treatment can regulate lipid metabolism, improve the intrinsic environment of fatty liver, reduce the level of transaminase, and the clinical efficacy is better than the pure western medicine treatment.

5. Conclusion

In summary, the etiology of NAFLD may be the result of the joint action of many aspects, including obesity, insulin resistance, intestinal flora imbalance and other exogenous factors, but also may be related to the genetic closeness of FALD patients and inherent immune imbalance, which can induce the disease through a series of factors. The specific etiology and pathogenesis of NAFLD have not been fully elucidated, and the treatment of NAFLD is mainly based on symptomatic treatment, such as reducing weight, controlling blood glucose, controlling blood lipids, etc. Nowadays, it is found that some of the components of traditional Chinese medicines can

effectively improve the liver function, alleviate the progression of hepatic fibrosis, reduce the accumulation of hepatic fat, alleviate the hepatic injury and enhance the recovery of the liver. Liver recovery. External treatment of Chinese medicine can help to improve the efficacy of traditional Chinese medicine and western medicine, and can improve the overall resistance of patients and slow down the development of the disease, therefore, the combined application of Chinese medicine and Chinese medicine gongfu can be used as a research direction in the future, and the treatment of NAFLD by Chinese medicine has a broad prospect.

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