

Progress of Clinical Research on Prevention and Treatment of Type 2 Diabetes Mellitus with Nonalcoholic Fatty Liver by Traditional Chinese Medicine

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Abstract: Both type 2 diabetes mellitus (T2DM) and nonalcoholic fatty liver (NAFLD) are metabolic diseases, which often affect each other and occur simultaneously. Insulin resistance is the common pathogenesis of both. According to the pathogenesis and clinical manifestations of T2DM with NAFLD, modern doctors classify it as "diabetes disease" combined with "accumulation" or "hypochondriac pain". It is believed that the disease is mainly related to congenital deficiency, improper diet, poor mood and excessive work and rest. Disease location involves liver, spleen, kidney three viscera, disease is mostly the deficiency of the deficiency of liver, spleen and kidney, qi stagnation, blood stasis, phlegm-dampness obstruction as the standard. Give full play to the unique advantages of the whole concept of TCM and the thought of syndrome differentiation and treatment, so as to reduce symptoms, reduce recurrence and regulate the metabolism of the body. In recent years, new progress has been made in the study of T2DM complicated with NAFLD by traditional Chinese medicine. Now, the etiology and pathogenesis of T2DM complicated with NAFLD are systematically reviewed, which provides new ideas for the clinical diagnosis and treatment of T2DM complicated with NAFLD.

Keywords: Type 2 diabetes mellitus complicated with nonalcoholic fatty liver, Traditional Chinese medicine, Clinical research progress.

1. Introduction

With the continuous development of social economy, people's eating habits and lifestyle have undergone great changes, and the incidence of metabolic diseases such as type 2 diabetes and fatty liver is also increasing year by year. T2DM and NAFLD often coexist, increasing the occurrence of diabetes complications and the possibility of liver damage. Long-term metabolic disorders will further lead to the damage of multiple organs and tissues throughout the body, increasing the risk of multiple diseases. In modern medicine, there is no specific treatment for T2DM complicated with NAFLD. The main treatment methods are hypoglycemic, weight loss, liver protection and other palliative treatments, which are costly and cannot achieve the curative effect. Therefore, TCM treatment and research on T2DM complicated with NAFLD have unique advantages.

2. Etiology and Pathogenesis

Type 2 diabetes belongs to traditional Chinese medicine "Xiaothirst", "Xiaozhong", "Xiaoheat" and other categories, non-alcoholic fatty liver disease in traditional Chinese medicine has no corresponding disease name, but it can be classified as "fat qi", "hypochondriac pain", "accumulation" and other categories according to its pathogenesis characteristics and clinical manifestations. Although there is no specific corresponding disease name and clear etiology and pathogenesis analysis in ancient medical books, doctors currently classify it as "Xiaothirst", "fat qi", "liver fetishism" and other categories according to its pathogenesis and clinical manifestations. Liu Huaizhen et al. [1] believed that the pathogenesis of T2DM complicated with NAFLD was liver depression and spleen deficiency and internal obstruction of

phlegm and blood stasis. Spleen-yin two deficiency, spleen transport weak, Sheng Qing down turbid loss; The deficiency of liver Yin and the use of Yang by liver body Yin will cause the function of the liver master to relieve and regulate qi. Soil does not lift wood, wood does not drain soil, liver loss of drainage, Qi machinery is not smooth, water grain fine transport disorder and internal phlegm dampness, accumulated long heat, phlegm, dampness, heat, stasis mutual occurrence of this disease. Lu Bo [2], the chief physician, believed that improper diet was the main cause of T2DM complicated with NAFLD. Excessive eating fat, thick and greasy, resulting in stomach not master to accept, Yangming gastrointestinal heat and dryness injury, spleen master transport and dereliction, wet turbid endogenous. Heat blazing gastrointestinal, damp-heat trapped spleen, long then phlegm and blood stasis interjunction, hair for this disease. Therefore, the pathogenesis of this disease is summarized as "stomach heat and spleen depression, phlegm turbidity-stasis" [3]. Bai Jin-shang [4] believed that spleen-kidney Yang deficiency was the main pathological basis of T2DM complicated with NAFLD. Type 2 diabetes combined with non-alcoholic fatty liver is developed on the basis of type 2 diabetes, the course of the disease is long, injury and kidney Yang, spleen Yang root in the kidney, spleen kidney Yang deficiency, spleen deficiency wet turbidness endogenous, chronic heat, damp-heat accumulation of liver and gallbladder, liver loss of storage and drainage, Qi machinery is not smooth, resulting in damp-heat, phlegm turbidness, blood stasis in the hypochthmia, resulting in the occurrence of the disease. It is concluded that the deficiency of spleen and kidney Yang is the basic pathogenesis of this disease. Qi stagnation of the liver is an important link. Dampness-heat, phlegm and blood stasis are the pathogenic factors and the key to its pathogenesis. Wang Jueyun [5] et al. believed that improper diet and lack of exercise were the main causes of T2DM complicated with

NAFLD. Excessive eating fat thick greasy, sedentary, phlegm and dampness, resulting in middle jiao spleen and stomach rise and fall, not on the mouth mouth dry, thirsty; Long-term diet is not proper, breeding phlegm dampness, resulting in spleen master transport and dysregulation, spleen does not transport, phlegm dampness is even worse, phlegm dampness affects the operation of Qi and blood, for a long time, phlegm and blood stasis are intertwined, remaining in the hypochetus, liver dredge dereliction of duty, it is the disease. Guo Fengnian [6] believed that the common causes of T2DM combined with NAFLD were improper diet, less activity from work and rest, emotional discomfort and old age. Its main pathogenesis is phlegm and dampness. Liver and spleen renal dysfunction, spleen loss of transport, sputum turbid endogenous; Liver loss and drainage, qi stagnation and blood stasis; Kidney deficiency strain, water transport is unfavorable. Qi stagnation, phlegm and blood stasis run through the whole process of the occurrence and development of the disease. Liu Xueyan et al. [7] believed that turbidity toxin was the core pathogenesis of T2DM complicated with NAFLD. Excessive diet, obstructed grain qi in the middle jiao, too much stomach absorption, insufficient spleen transport, poor water and grain transformation, and turbidity toxin formation were the causes of the disease.

To sum up, the occurrence of type 2 diabetes combined with nonalcoholic fatty liver is related to innate endowment, dietary sentiment and work-rest balance. Most of the disease is the deficiency of the deficiency of liver, spleen and kidney, qi stagnation, blood stasis, phlegm and dampness each become the standard. Mainly involved in liver, spleen, kidney three viscera, spleen deficiency and dampness, phlegm and blood stasis each become the main pathological basis.

3. Chinese Medicine Treatment

At present, Western medicine usually takes liver protection and enzyme lowering, glucose lowering and lipid lowering as the main treatment options for T2DM complicated with NAFLD. However, due to the single drug target and potential risks of long-term use, the holistic concept and syndrome differentiation of Chinese medicine have significant advantages in the treatment of T2DM complicated with NAFLD.

3.1 Syndrome Differentiation and Treatment

Qian Xiaoqing et al. [8] believed that T2DM complicated with NAFLD was mainly caused by the syndrome of phlegm-heat intercombination, and the treatment was based on clearing heat and dampness, regulating qi and resolving phlegm, and Huanglian Wendan Decoction was used as the prescription (drug composition: Coptis, Huangqin, Qingpinellia, bamboo Ru, Zedoary, Tangerine peel, Thunberg Fritillaria, Poria, stir-fried white bamboo, Bupleurum, Gualou, Pueraria, Salvia miltiorrhiza). Chief physician Lu Bo [9] inherited the academic thought of Mi school and based on Yangming theory on the treatment of diabetes disease, proposed that the main pathogenesis of T2DM complicated with NAFLD was stomach heat and spleen distress, phlegm turbidness and stasis, and self-prepared Yunpihua Turbidus prescription (Coptis, Scuaria baicaleae, Yujin, Qingpinellia, dried ginger, Codonopsis, Allium Macrostemon, Salvia Miltiorrhiza, white

Peony, Chuanxiong, and Sheng Hawthorn). The treatment of T2DM complicated with NAFLD was innovatively proposed. Zou Yaowu [10] believed that the core pathogenesis of this disease was liver depression and spleen deficiency, and the treatment should be based on soothing the liver and strengthening the spleen, eliminating phlegm and removing blood stasis. It is suggested that Acorus Yujin decoction should be used in the treatment of T2DM patients with liver depression and spleen deficiency complicated with NAFLD, including Acorus calamus, stir-fried gardenia, fresh bamboo leaves, peony bark, raw ground, Astragalus, Bupleurum, Yu Jin, forsythia, Dengxin, Mutong, Salvia miltiorrhiza, Tuckaia and pale bamboo li. Director Wu Shentao [11] constantly summarized clinical experience and proposed turbidio-detoxification method to treat T2DM complicated with NAFLD based on turbidio-toxin therapy theory, and self-designed turbidio-detoxification formula (rigidopsis, cicada, turmeric, rhubarb, Bupleurum, Coptis, scutellaria, Hoshi, Paeoniae, and Perilan). The formula was made from Tiger-lowering SAN combined with Da Chaihu Decoction, focusing on regulating the spleen and stomach qi mechanism to coordinate the lifting and lowering. It has achieved the effect of treating diseases by preventing internal turbid poison. Professor Ling Xiangli [12] summarized clinical experience and believed that Qi and Yin deficiency and phlegm turbidity and blood stasis were the main pathogenesis of this disease. He created his own experience prescription Tangtongyin (Rehmannia, Yam, Fructus officinalis, Poria, Zexia, Danpi, Radix Astragalus, Radix Gupi, Saltiorrhiza, and Cassia sinensis), which has the effect of tonifying qi and Yin, removing blood stasis and removing turbidity, and has good clinical efficacy in the treatment of T2DM complicated with NAFLD.

3.2 Specific Treatment

Ning Meilian [13] randomly divided the patients with T2DM containing phlegm and NAFLD conforming to liver-stagnation and spleen-deficiency into treatment group and control group, with 20 cases in each group. The control group was given lifestyle intervention and basic Western medicine treatment, and the treatment group was additionally given decoction Shugan Huatan and Turbide-lowering (Bupleurum bupleurum, pinellia pinellia, Radix paeoniae sinensis, Angelica sinensis, atractyloatractyloides, Radix tangerine peel, poria coicae, Radix coicae seed) on the basis of the control group. Alisma purpurea, Salvia miltiorrhiza, Radix miltiorrhiza, Fructus trichosanthis, Radix Pueraria, Radix Coptis). Result: After treatment, glycemic index (FPG, 2HPG, HbA1C), blood lipids (TC, TG, LDL-C, HDL-C), liver function level (ALT, AST, GGT), insulin resistance index, fasting insulin, tumor necrosis factor-alpha and interleukin-6 were all improved in both groups compared with before treatment. The total effective rate of the treatment group was significantly better than that of the control group. Zhao Siyang [14] et al. divided T2DM patients with NAFLD into control group and observation group according to randomized control method, with 35 cases in each group. The control group was treated with metformin, and the observation group was treated with Jinlida granule on the basis of metformin. Results: After 12 weeks of treatment, the level of glucose and lipid metabolism, insulin level and liver function in the observation group were significantly improved compared with the

treatment group. The proportion of mild NAFLD in the observation group was higher than that in the control group, and the proportion of moderate and severe NAFLD in the control group was higher than that in the observation group. Shen Yingge [15] et al selected 80 patients with spleen deficiency and blood stasis type T2DM complicated with NAFLD and randomly divided them into control group and experimental group, 40 cases in each group. Patients in both groups were given symptomatic treatment such as hypoglycemic, hypertensive and lipid-lowering based on lifestyle intervention. On this basis, the treatment group was given oral Jianpi Yiqi Tongluo decoction (Astragalus, Poria, Codonopsis, Baizhu, Angelica, Chuanligong, salvia miltiorrhiza, wood fragrance, Bupleurum, turmeric, gynostaphylla, schisandra, pueraria, licorice). Result: The experimental group was significantly superior to the control group in reducing serum levels of HOMA-IR, HbA1c, TG, LDL-C, FFA, etc. After treatment, the TCM symptom score and serum TNF-alpha and IL-6 levels of the treatment group were lower than those of the pre-treatment and the control group at the same period, and the serum APN level was significantly higher than that of the pre-treatment and the control group at the same period. The total effective rate of Jianpi Yiqi Tongluo prescription group (94.9%) was significantly higher than that of control group (65.8%). Wang Xiaoqian [16] divided 60 patients who met the inclusion criteria into control group and observation group, with 30 patients in each group. The control group was given general treatment and western medicine treatment, and the observation group was given Gegen Qinlian Xeliu prescription (Pueraria, Radix pseudostellariae, Radix Baizhu, Pinellia pinellia, safflower, Scutellaria scutellaria, Radix Coptis, Radix bupleuri and Radix Paeoniae) on the basis of this treatment. Results: BMI, WHR, blood glucose and insulin related indexes (FPG, 2hPG, HbA1c, FINS, HOMA-IR), blood lipids related indexes (TG, TC, LDL-C) and liver function related indexes (ALT, AST) in the observation group were significantly reduced compared with those in the control group, and liver B-ultrasound classification in the observation group was more significantly improved. Liu Yangyang [17] believed that spleen deficiency and excessive dampness and phlegm-stasis interformation were the main etiology and pathogenesis of modern type 2 diabetes mellitus. 60 selected T2DM patients with NAFLD were randomly divided into two groups on average. The control group was given basic treatment, and the observation group was additionally treated with Qihuang Jiangturu granules (Astragalus, rhubarb, salviashen, alisma, poria, cassia seed, pueraria root, and kelp). Results: The improvement of blood glucose, blood lipid, glycosylated hemoglobin, liver function and total effective rate in observation group were higher than those in control group. Conclusion: Qihuang Jiangturu Granule is effective in the treatment of T2DM complicated with NAFLD, and can effectively reduce blood sugar, blood lipids, liver function and other indexes.

3.3 Acupuncture Treatment

Acupuncture treatment has the characteristics of small adverse reaction, simple and effective. On the basis of syndrome differentiation, selecting appropriate acupoints and applying different acupuncture methods can regulate the functions of the body's five viscera and six organs and

improve the disorder of glucose and lipid metabolism.

Acupuncture therapy has the function of dredging meridians, regulating the qi and blood of zang-fu organs, and thus improving the endocrine disorder of the body. Li Qin [18], under the guidance of Professor Ni Qing, summarized in a large number of clinical practices that acupuncture and moxibustion treatment of type 2 diabetes mellitus complicated with non-alcoholic fatty liver mainly used Zhongwan, Zusanli, Fenglong, Sanyinjiao, Taichong and other acupoints, and added or subtraction acupoint prescriptions and selected different acupuncture methods according to clinical dialectics and personal physical differences. It can regulate the function of viscera and the disorder of glucose and lipid metabolism, and has achieved good clinical effect. Xue Li et al. [19] randomly divided 60 T2DM patients with NAFLD into control group and treatment group with 30 patients in each group. Both groups were given basic diabetes treatment, the control group was given Zhibituo tablet on the basis of which, and the treatment group was given acupuncture treatment (Quchi, Hegu, Zhongwan, Zusanli, Fenglong, Yinlingquan, Sanyinjiao, Xuehai, Diji, etc.). The results showed that the improvement of blood glucose, blood lipids and glycated hemoglobin in the treatment group was better than that in the control group, and the effective rate was significantly higher than that in the control group. Conclusion: Acupuncture treatment can not only improve the symptoms of T2DM patients with NAFLD, but also improve the blood glucose, blood lipids and liver function of patients to a certain extent, and can delay the development of the disease. Cui Yanglin et al. [20] believed that both type 2 diabetes and non-alcoholic fatty liver disease had phlegm-moisture intrinsic syndrome. He selected 60 patients with T2DM complicated with NAFLD phlegm-moisture intrinsic syndrome and randomly divided them into two groups. The control group was treated with oral polyene phosphatidylcholine capsules and metformin hydrochloride tablets. On the basis of this treatment, the other group was treated with oral plus minus Erchen decoction combined with meridian injection acupuncture (Dadu point, Sanyinjiao point, Zusanli point, Shangqiu point, Yinlingquan point, Diji point, Fenglong point, water point, etc.), acupuncture once every other day. Results: After 8 weeks of treatment, blood glucose, blood lipid, liver function index, adiponectin and liver imaging performance in the treatment group were better than those in the control group.

4. Problems and Prospects

Diabetes mellitus combined with nonalcoholic fatty liver is a chronic metabolic disease, its pathogenesis is not clear at present, Western medicine has no specific drugs for this disease, mainly to reduce blood sugar, weight loss, liver protection and other treatments. A comprehensive study has reported relevant literature on the treatment of T2DM complicated with NAFLD by traditional Chinese medicine. Clinical methods such as syndrome differentiation, prescription treatment and acupuncture can alleviate symptoms, improve insulin resistance, reduce blood sugar, blood lipids, glycated hemoglobin and other indicators of patients, and improve the quality of life of patients. It shows the advantages and prospects of traditional Chinese medicine in treating T2DM with NAFLD. However, at present, the research reports on TCM treatment of T2DM complicated

with NAFLD are all famous doctors' experience prescriptions of clinicians, lack of systematic treatment standards, large sample systematic studies, lack of animal experiments, different evaluation criteria for efficacy, and difficult follow-up observation. In response to the above problems, multi-center, large-sample clinical randomized controlled trials should be carried out to establish standard clinical trial protocols to provide strong scientific support for clinical practice, so that traditional Chinese medicine can play a greater role in the treatment of type 2 diabetes mellitus combined with non-alcoholic fatty liver disease.

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