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Research Progress of Integrated Traditional Chinese and Western Medicine in the Treatment of Early Diabetic Nephropathy

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Abstract: ***Diabetic nephropathy (DN) is a specific damage of diabetes, early DN can be manifested as microproteinuria, the symptoms are insidious, not easy to be detected, it will cause irreversible damage to the kidneys in a short period of time, and it can develop into kidney failure with the gradual progression of the disease, which seriously threatens the health of patients. Therefore, early intervention and effective treatment are crucial to reverse kidney damage and delay the progression of the disease. This article analyzes the literature on the treatment of DN in recent years, and clarifies that the combination of traditional Chinese and Western medicine has an ideal effect in the treatment of early DN, in order to provide reference for the clinical treatment of DN.***

Keywords: Consumptive thirst, Early diabetic nephropathy, Integrated traditional Chinese and western medicine**.**

1. Introduction

In recent years, with the general improvement of people's living standards, the impact of fast-paced lifestyles, high-stress work rhythms, and rich dietary structures, the incidence of diabetes has increased year by year, and the survey [1] shows that the global prevalence of diabetes is estimated to increase to 10.2% (578 million people) by 2030 and to 783 million by 2045 [2]. The prevalence of diagnosis of kidney disease in patients with type 2 diabetes mellitus in China is 20%-60%, and DN is one of the most serious complications of diabetes mellitus and an important cause of death for it. Early DN belongs to stage III, that is, the microalbuminuria stage, its symptoms are insidious and not easy to be detected, and the disease will progress to the middle and end stages without the patient being aware of it, causing irreversible consequences and seriously affecting the quality of life and survival time of patients. Therefore, early intervention and treatment of the disease are very crucial, and if we can detect the kidney damage of diabetic patients in time and give appropriate treatment in time, the damage to the kidney can be greatly reduced or reduced [3]. In recent years, the clinical research on the treatment of early DN with integrated traditional Chinese and Western medicine has been continuously explored and some progress has been made, which is summarized as follows.

2. Awareness of early DN

2.1 Traditional Chinese Medicine Etiology and Pathogenesis

There is no clear name of "diabetes nephropathy" in traditional Chinese medicine, which can be attributed to such categories as "kidney elimination", "turbid urine" and "edema" in traditional Chinese medicine according to symptoms [4]. Zheng Nan [5] proposed in the book "Research on diabetes nephropathy (Diabetic Nephropathy)" that the disease of DN is called "DN" in Chinese medicine, and clearly pointed out that its primary cause is the basic cause of diabetes, and the disease location mainly involves the kidney. The ancient medical books have also recorded many descriptions of the etiology and pathogenesis of DN. The Yellow Emperor's Internal Classic regards the deficiency of the internal organs, excessive fat and sweet taste, and emotional discomfort as the causes, and internal heat as the main pathogenesis. Because DN is based on the original onset of diabetes, diabetes has a long course and takes a long time. It consumes more yin qi of the body, and it is easy to reach the kidney after a long illness. If the kidney is deficient, it will be blocked and lost, and the essence will flow out, showing proteinuria; However, if the kidney essence is released, it cannot be nourished by the spleen. Spleen deficiency is not conducive to the circulation of water and grain essence, resulting in excessive accumulation of phlegm and dampness in the body. Phlegm turbidity flows into the blood vessels, blocking the blood vessels and causing poor blood flow, leading to blood stasis, kidney meridian stasis, sinking of qi, lack of control, and slight loss of water and grain essence can lead to changes in urination, reduced appetite, fatigue, and soreness in the waist and knees. Good temperament and good fortune are the basis for the normal distribution of water, grain, and essence. The kidneys store the essence of innate reproduction and the essence of acquired organs, so the spleen and kidneys play an important role in the development and changes of diseases.

Modern medicine is combined with the living environment, and the major physicians have different understanding of the etiology and pathogenesis of DN. Professor Xie Chunguang's understanding of the pathogenesis of early DN emphasizes the deficiency of both qi and yin as the foundation, which belongs to kidney deficiency and collateral stagnation in the early stage, and kidney deficiency and blood stasis in the late stage [6].Professor Lv Renhe put forward the pathogenesis theory of DN "mini mass syndrome" [7], and believed that DN was caused by the mistreatment of diabetes. Yin deficiency, dryness and heat hurt qi and yin for a long time, and phlegm, heat, depression, and blood stasis were stuck together in the kidney collateral. Later, it gradually became a mass syndrome. Academician Tong Xiaolin [8] believed that strengthening fire and eating qi, damaging yin and consuming qi, led to

kidney qi loss, kidney collateral stasis, and a small amount of fine discharge, which developed into DN. Zhang Daning, a master of traditional Chinese medicine [9], believes that the basic pathogenesis of early DN is deficiency, blood stasis and dampness. The deficiency of both qi and yin in the spleen and kidney, deficiency of both kidney and blood stasis run through the whole process, and the development of the disease is aggravated by the lingering dampness and phlegm. Professor Yan Li [10] believes that the basic pathogenesis of DN is liver loss, blood loss, fluid deficiency and yin deficiency, and blood stasis throughout. Professor Zou Yanqin [11], a master of traditional Chinese medicine, believes that the core pathogenesis of DN is spleen and kidney deficiency, with dampness and blood stasis blocking collaterals as the standard, and emphasizes the key role of dampness and blood stasis in disease development. In a word, the causes of early DN are mostly congenital endowment deficiency, improper diet, emotional imbalance, excessive fatigue, treatment failure and mistreatment. The main disease location is the kidney, which is based on deficiency and excess, yin deficiency, phlegm, dampness and blood stasis.

2.2 Pathogenesis of Western Medicine

Early DN showed high perfusion, high filtration rate and changes in glomerular filtration barrier, which led to the occurrence and development of microalbuminuria. The pathogenesis of DN is relatively complex and has not been particularly clear. At present, it is generally believed that genetic factors, abnormal glucose and lipid metabolism and hemodynamics are the main reasons for the occurrence of DN.A large number of other studies have shown that the abnormal expression of inflammatory reaction, cytokines and chemokines plays a key role in the occurrence and development of DN [12]. When the patient is in the state of hyperglycemia for a long time, the body will produce a large number of proinflammatory factors and inflammatory mediators, attacking the renal tissue cells, thus aggravating the renal damage of diabetes [13]. In addition, there are mechanisms such as autophagy and endoplasmic reticulum stress, which together affect the pathogenesis of diabetes and its complications DN. Research has shown that continuous oxidative stress can cause the accumulation of reactive oxygen species, leading to the production of numerous cytokines and extracellular matrix, ultimately resulting in renal fibrosis [14]. Autophagy, as a type of lysosomal degradation pathway, is an important component of maintaining normal physiological functions in cells. It maintains the homeostasis of cells under stress, and the decrease in autophagy activity of renal intrinsic cells can increase renal damage [15].

3. Treatment of the early DN

3.1 Traditional Chinese Medicine Treatment

3.1.1 Traditional Chinese Medicine Compound Treatment

In recent years, with the further development of early DN, doctors have summarized practical prescriptions and treatment methods in the accumulation of clinical applications. Traditional Chinese medicine has achieved satisfactory results in treating this disease, with unique advantages in improving clinical symptoms, regulating glucose and lipid metabolism, reducing urinary protein, alleviating inflammatory reactions, and delaying disease progression in DN patients.

Shi Qian [16] used Shengmai San and Liuwei Dihuang Decoction (prepared rehmannia root, codonopsis pilosula, scrophularia root, astragalus root, coptis root, ophiopogon japonicus, schisandra chinensis, yam, atractylodes macrocephala, poria, rhizoma alismatis, peony bark, cornus officinalis) to treat 60 patients with early DN of the type of deficiency of both qi and yin. The research results showed that the combination of Shengmai San and Liuwei Dihuang Decoction on the basis of conventional western medicine can nourish kidney yin, replenish qi, generate fluid, promote blood circulation and remove stasis. The combination of these drugs can improve the clearance rate of endogenous creatinine, thus reduce the ratio of urinary protein to creatinine, and improve renal function; At the same time, peony bark, yam, Poria cocos, and Codonopsis pilosula all have significant anti-inflammatory effects, which can reduce inflammatory reactions in the body and improve clinical efficacy. Tan Miao et al. [17] used Jiawei Ascendant (Rhubarb, Turmeric, Zombie Silkworm, Cicada Molt, Coptis chinensis, Astragalus membranaceus, Rehmannia rehmannia and Poria cocos) to treat early DN with qi and yin deficiency, turbidity and toxicity and depression syndrome, and the study showed that Jiawei Ascending Ascendant can significantly reduce the effects of glycotoxicity and lipid toxicity on the kidneys, reduce glycosylated hemoglobin, blood lipids, and renal tubular function markers, alleviate the early renal tubular injury in patients, and inhibit the activation of NADPH oxidase 4 and enhance the activity and expression of antioxidant enzymes to regulate the body's oxidative-antioxidant system, reduce oxidative stress and improve kidney function. Yu Feiya et al. [18] used the self prepared Qishen Bushen Huoxue Decoction to treat 35 patients with early DN. The prescription contains astragalus, salvia miltiorrhiza, poria cocos, alisma orientalis, prepared rehmannia root, stir fried yam, cornus officinalis, stir fried Chuanduan, achyranthes bidentata, dodder seed, wolfberry fruit, Chuanxiong, patrinia, Euryale, and Rosa laevigata fruit. The results show that the combination of Qishen Bushen Huoxue Decoction on the basis of conventional western medicine can improve patients' clinical symptoms, reduce urinary protein excretion, regulate glycolipid metabolism, and maintain the stability of renal function. Ding Jingxian et al. [19] used tonifying kidney and invigorating blood and draining turbidity decoction (Astragalus membranaceus, Rehmannia rehmannia root, Rhubarb rhubarb, Morinda officinalis, yam, Cornus officinalis, Salvia miltiorrhizae, safflower, peony bark, Acacia japonica, Poria cocos, Ze Yuan) to treat early type 2 DN with qi and yin deficiency and stasis internal suspension, and found that the tonifying kidney and invigorating blood and draining turbidity decoction can improve the clinical efficacy, alleviate clinical symptoms, improve renal function, and reduce the expression level of inflammatory factor indexes (serum TGFβ1, MCP1, sICAM1, IL17), which is worthy of clinical promotion. Tongluo Hu Shen Tang is composed of six hypoglycemic formulas (Huangqi, Shengdi, Cangzhu, Xuanshen, Gegen, Codonopsis pilosula) developed by Professor Zhu Shenyu, along with herbs such as Yimucao, Baimaogen, Xuduan, Chuanxiong,

and Jixueteng, which promote qi cooling, blood circulation, and blood circulation. Research shows that Tongluo Hushen Decoction can reduce the levels of urea nitrogen, blood creatinine, urinary microprotein, endothelin-1, and thromboxane B2 in the treatment of early type 2 DN, and can significantly improve microcirculation, reduce urinary protein, and protect the kidney [20].

3.1.2 Traditional Chinese patent medicines treatment

The efficacy of Chinese medicine is mild, and the toxicity and side effects are relatively small, and it can help to reduce urine protein and protect kidney function in the treatment of early DN.

Qizhi Yishen Capsule is mainly composed of Astragalus membranaceus, leech, fried zombie silkworm, turtle insect, ligustrum seed, Qingfeng vine, Rehmannia and other traditional Chinese medicines, which have the effect of replenishing qi and nourishing yin, dissolving blood stasis and channeling. Jiang Chen et al. [21] observed a multi-center prospective study of Qizhi Yishen Capsule in the treatment of Qi and Yin deficiency syndrome in early DN, and found that oral Qizhi Yishen Capsule can effectively reduce the urinary albumin excretion rate and 24-hour urine protein quantification after 24 weeks of treatment, maintain the stability of glomerular filtration rate, protect kidney function, and alleviate symptoms such as clinical fatigue, dry mouth and tongue, which is safe for clinical use.Lao Xiaoqing et al. [22] established a DN mouse model by injecting small doses of streptozotocin multiple times, and observed the improvement effect and possible mechanism of Qishi Shenshu Capsule on renal fibrosis in DN mice. It is mainly composed of various traditional Chinese medicines such as Astragalus membranaceus, Rehmannia glutinosa, Leonurus heterophylla, leech, Shiwei, centipede, and has the effects of clearing heat and dampness, relaxing collaterals and promoting blood circulation, and nourishing qi and consolidating kidneys. The results of the study showed that Qishi Shenshu Capsules have a renal protective effect independent of blood glucose control, reducing damage to podocytes; It can also alleviate the pathological changes of renal fibrosis in DN, and its mechanism may be related to the inhibition of the expression of TFG -β1/Smad2/3 signaling pathway.

Niaoduqing Granule are composed of rhubarb, astragalus, mulberry bark, Poria cocos, Atractylodes macrocephala, Paeonia lactiflora, Salvia miltiorrhiza, Plantago asiatica, Sophora flavescens, and Polygonum multiflorum. They have the functions of promoting blood circulation and removing blood stasis, strengthening the spleen and removing dampness, and clearing the organs and reducing turbidity. Clinical research shows that Niaoduqing Granule can increase the levels of superoxide dismutase and glutathione peroxidase, reduce the level of malondialdehyde, and alleviate the oxidative stress reaction of early DN patients [23]; It can also reduce the secretion of inflammatory factors and alleviate the state of micro inflammation, which may be related to the anti-inflammatory effects of rhubarb, plantain seeds, Poria cocos, and other ingredients in the Niaoduqing Granule [24]. From this, it can be seen that Uremic Clearance Granules can treat DN through multiple pathways and targets, such as antioxidant stress, anti-inflammatory, kidney protection, and improving blood circulation, effectively improving kidney function and preventing or delaying disease progression [25].

3.1.3 External treatment of traditional Chinese medicine

External treatment of traditional Chinese medicine, that is, the treatment of drugs without oral administration, mainly includes acupuncture and moxibustion, fumigation and washing of traditional Chinese medicine, point injection, point application, enema, etc.

Li Bing et al. [26] treated early DN with Peiyuan Yishen Tongluo Recipe combined with acupuncture and moxibustion. The control group was treated with conventional western medicine, and the observation group was treated with Peiyuan Yishen Tongluo Recipe combined with acupuncture and moxibustion on the basis of the control group. The results showed that the total effective rate of the observation group was higher than that of the control group ($P<0.05$), indicating that this method had significant effects on early DN, especially in improving patients' blood sugar and renal function levels. By injecting medication into acupoints, physical stimulation can be applied to the patient's acupoints, which can have effects such as activating collaterals and promoting muscle circulation, as well as lifting and lowering qi machines. Ji Zhirong [27] applied the combination of ShengJiang San and acupoint injection to treat 98 patients with early DN. The control group was treated with the western medicine enalapril hydrochloride tablets, while the observation group was treated with the combination of ShengJiang San and acupoint injection. The acupoints were selected at Zusanli and Shenshu, and Huangqi injection was used for injection. The results showed that the combination of ShengJiang San and acupoint injection can achieve the effect of orderly elevation and elevation, as well as the balance of internal and external ketones in the upper and lower parts. At the same time, it can effectively protect the renal function of patients and alleviate the development of the disease.

3.2 Western Medicine Treatment

At present, modern medical treatment for early DN mainly starts with limiting the intake of crude protein, increasing physical activity, changing lifestyle, and reducing the intake of carbohydrates, salt, and fats as much as possible to lower blood pressure, lower blood sugar, and regulate fat. Combined treatment with drugs that improve renal microcirculation is used to delay the progression of kidney disease as much as possible. The main purpose of treatment is to delay kidney damage.

Therapeutic drugs include DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, renin - angiotensin - aldosterone system antagonists, nonsteroidal mineralocorticoid receptor antagonists, etc. Among them, angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor antagonist (ARB) antihypertensive drugs can effectively reduce urinary protein, and are currently the first-line treatment drugs for DN. However, ACEI drugs have side effects such as irritating dry cough, so ARB drugs are often used clinically, represented by valsartan, irbesartan and other drugs. SGLT2 inhibitors can lower the renal glucose

threshold, inhibit the reabsorption of glucose by the proximal tubules, promote the excretion of urinary glucose, and achieve the goal of lowering blood sugar. They also have protective and antihypertensive effects on the kidneys. Lu Haibo et al. [28] treated 90 patients with early DN with combination therapy of levocarnitine and empagliflozin. After 3 months, they found that the mechanism of action of combination therapy of levocarnitine and empagliflozin should be related to the decrease in serum sICAM-1 expression level and the increase in serum CTRP9 expression level. It can significantly enhance the clinical symptoms of patients, reduce the levels of inflammatory factors, and restore renal function. Yuan Yimeng [29] treated 92 patients with early DN. The control group was treated with irbesartan combined with insulin glargine, and the study group was treated with dulaglutide, a weekly preparation of GLP-1 receptor agonist, on the basis of the control group. The results showed that the renal function indicators, glucose metabolism indicators, islet function, and the incidence of hypoglycemic events in the study group were superior to the control group, that is, dulaglutide, a weekly preparation of GLP-1 receptor agonist, had obvious efficacy and high safety in treating early DN, which can be used for reference in clinical treatment.

3.3 Integrated Treatment of Chinese Medicine and Western Medicine

The combination therapy of Chinese and Western medicine is widely used in early DN patients. Western medicine can quickly regulate various indicators of the body, supplemented by traditional Chinese medicine intervention to improve symptoms and signs. It can fully leverage the respective advantages of Chinese medicine and Western medicine, and have a positive effect on promoting the physical and mental health of patients.

Liu Decui et al. [30] used Jinshuibao combined with pancreatic kininogenase to treat early DN patients. After 3 months, the levels of blood glucose, creatinine, urea, and urinary microalbumin all decreased, proving that Jinshuibao combined with pancreatic kininogenase can improve the treatment effect, protect kidney function, and delay disease progression in early DN. Xue Jianguo [31] conducted a clinical observation on the treatment of early DN patients with Danhong injection combined with valsartan. The results showed that Danhong injection combined with valsartan could reduce the patient's urea nitrogen, urinary microalbumin to creatinine ratio, and blood creatinine index levels. The synergy of the two could regulate the patient's blood rheology, thereby inhibiting urinary albumin excretion, improving renal function, and slowing down the severity of the disease. Wang Haiyan et al. [32] used Bailing Capsules combined with Dapagliflozin to treat 103 cases of early diabetic nephropathy. The patients' glucose metabolism indicators, renal function indicators, and oxidative stress indicators all decreased to a certain extent. Therefore, Bailing Capsules combined with Dapagliflozin can improve patients' blood glucose levels, renal function, oxidative stress status, and clinical symptoms, and alleviate inflammatory reactions. Chen Yujie et al. [33] used Huangkui capsules in combination with Dapagliflozin to treat 96 patients with early DN damp heat syndrome. The results showed that the two drugs complemented each other and could promote urinary sugar excretion while reducing patient inflammation, thereby improving renal function.

4. Conclusion

In recent years, the number of diabetes patients around the world is increasing gradually. The chronic increase of long-term blood sugar damages large and small blood vessels and endangers the heart, brain, kidney, peripheral nerves, eyes, feet, etc., of which DN is the most serious. Therefore, active intervention and treatment of diseases are very critical. If we can find the kidney damage of diabetes patients in time and give appropriate treatment, we can greatly reduce or reduce the damage to the kidney. Although Western medicine treatment methods are effective, they may have some side effects and limited clinical application, often treating the symptoms rather than the root cause. Traditional Chinese medicine treatment often focuses on regulation. Although the treatment process is slow, comprehensive clinical treatment can improve kidney function to a certain extent. The combination of Western medicine and traditional Chinese medicine can significantly improve clinical efficacy. Western medicine can lower blood sugar and lipid levels to control blood sugar and lipid stability, prevent the occurrence of other complications, and traditional Chinese medicine prescriptions can nourish qi, promote blood circulation, unblock collaterals, nourish the liver and kidneys, and treat both symptoms and root causes.

In summary, actively providing early DN patients with integrated traditional Chinese and Western medicine therapy can improve kidney function with significant effects. Through data research, we can find that in the future, early DN patients will be treated with integrated Chinese and western medicine, starting from the whole, individualized guidance, combination of traditional Chinese and western medicine, and the use of conventional western medicine plus TCM treatment based on syndrome differentiation. The two complement each other, which can effectively improve the treatment rate of patients, improve their renal function, effectively prevent the progress of complications in diabetes patients, improve their quality of life, increase the health index and happiness index of patients, and are worthy of clinical promotion.

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