

Research Progress on Synergistic Treatment of Diabetic Nephropathy with Chinese and Western Medicine

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Abstract: *Diabetic Kidney Disease (DKD) is a grave microvascular complication of diabetes mellitus, with a multifactorial pathogenesis involving metabolic disorders, hemodynamic alterations, oxidative stress, and inflammatory responses. Conventional Western medicine identifies hyperglycemia, hypertension, and activation of the renin-angiotensin system (RAS) as the fundamental pathological mechanisms. Treatment strategies prioritize blood glucose management (e.g., SGLT2 inhibitors, GLP-1 RA), blood pressure control (ACEI/ARB), and the delay of renal function deterioration. In contrast, Chinese medicine is predicated on the “five-organ rule,” which posits a connection between fluid metabolism and the dysfunction of the five organs. This approach aims to ameliorate symptoms and mitigate the adverse effects of Western medications by regulating the balance of yin and yang in a holistic manner.*

Keywords: Diabetic nephropathy, Achalasia nephropathy, Synergistic treatment of Chinese and Western medicine, Research progress.

1. Introduction

Diabetic Kidney Disease (DKD) is one of the most common microvascular complications of diabetes mellitus, and its prevalence is closely related to the duration of diabetes. According to national and international studies, the prevalence of DN in diabetic patients is about 20-40% [1], and it is noteworthy that the global incidence of DN has increased by 74% in the past 20 years, and it has become the leading cause of end-stage renal disease (ESRD), accounting for 30-50% of all ESRD cases in Europe, America and Japan. In the early stage of DN, it manifests only as microalbuminuria, which is easily neglected due to the lack of obvious symptoms. Once it enters the clinical proteinuria stage (urine protein ≥ 300 mg/g), kidney damage is irreversible. It takes about 8-12 years for the disease to progress from proteinuria to uremia, and the mortality rate is extremely high. At present, the treatment of diabetic nephropathy in Western medicine is mainly to control the progression of diabetic nephropathy by regulating blood glucose and changing lifestyle and dietary habits, and when it progresses to the uremic stage, only renal replacement therapy can be performed. This not only causes pain to patients, but also imposes a heavy financial burden on them and their families. Chinese medicine has unique advantages in the treatment of diabetic nephropathy through the understanding of its etiology and pathogenesis, based on the identification of evidence, and at the same time combined with some special treatments of Chinese medicine.

2. An Examination of Chinese Medicine's Approach to Diabetic Nephropathy.

2.1 Name of the Disease

Diabetic nephropathy has not been recorded in the Chinese medical text. According to its clinical manifestations, medical practitioners have referred to the early manifestations, such as frequent nocturnal urination, soreness and weakness of the waist and knees, etc., which are secondary to thirst, as

“Kidney Fading, Lowering Fading.” The middle and late stages, which are characterized by generalized edema, are referred to as “Oedema.” In the intermediate and late stages, the predominant presentations of generalized edema are designated as “edema,” while in the terminal stage, the primary manifestations of low urine output and dysuria are classified as “Guan Ge, Drowning Toxicity, Retention of Urinary Blanks”[2].

2.2 Knowledge of Etiology and Pathogenesis

2.2.1 Etiology

The prevailing school of thought among historical medical practitioners posits that the onset of ailments is associated with the body's vital energy and the encroachment of natural malevolence. The fullness of vitality cannot be compromised, and the deficiency of vitality must capitalize on the vulnerabilities of the external environment. The absence of positive qi has been linked not only to an individual's inherent constitution but also to the deprivation of sustenance. Collectively, these factors contribute to bodily transportation and failure, as well as transmission and distribution disorders. In the context of Chinese medicine, historical medical practitioners ascribed this etiology to numerous factors, including: 1) Insufficient innate endowment, the kidney is the birth of the body, the main body of yin and yang, the main collection of essence, and the main physiological function. Insufficient innate endowment leads to renal essence deficiency, loss of the solid, and leakage of urine [3]. 2) Six evils attack, six evils of the evils of the six evils attacked the human body, resulting in the human body qi and blood, yin and yang imbalance, thus developing the disease; 3) Dietary indiscretion: the spleen loses its ability to transport and transform. The long-term consumption of high-fat, sweet, and thick flavors can lead to a weakening of the spleen's transportation and transformation abilities. This results in the inability to provide the stomach with its essence, which is material rather than chemical in nature. Instead, it affects the spleen and stomach elevation function [4]. 4) Abnormal

emotions and moods. Concerns and ruminations have been shown to exert a detrimental effect on the spleen, while anger has been observed to inflict harm upon the liver. Furthermore, when the will is excessively pronounced, it has been demonstrated that this can lead to a disruption in the body's fluid equilibrium, which is susceptible to escalating into a state of thirst.

2.2.2 Disease Mechanisms

The pathogenesis of diabetic nephropathy remains a subject of debate among medical practitioners. However, a consensus has emerged regarding the fundamental mechanisms underpinning the condition. The disease is characterized by deficiency of the spleen and kidney, with phlegm-dampness and blood stasis as the symptoms. Feng Jianhua [5] posits that the fundamental cause of DN is the dysfunction of "spleen qi dispersing essence," and its clinical manifestations, such as proteinuria and edema, are attributable to the dysfunction of spleen qi dispersing essence. This is attributed to the fact that the spleen is unable to disperse essence, and both the spleen and kidneys are deficient. In contrast, Zhang Daning [6] proposes that the primary pathogenesis of diabetic nephropathy stems from kidney deficiency and blood stasis, with kidney deficiency serving as the predominant causative factor and blood stasis manifesting as a symptom. Professor Zhang Xikui has noted that the underlying mechanism of the disease is invariably associated with deficiencies of the spleen and kidneys, as well as with dampness, heat, blood stasis, and other factors throughout the course of the disease. These include phlegm, blood stasis, and turbid toxicity, as well as paralytic obstruction of collaterals, leading to damage to kidney collaterals and the subsequent onset of the disease [7]. Chai Kefu [8] posits that diabetic nephropathy can lead to its occurrence and progression, regardless of the external wind in the six external winds, or internal wind generated by the dysfunction of the liver and kidneys and other internal organs, yin and yang disharmony, and the change of yang qi hyper-reversal in the body. Zheng Huijuan et al. [9] propose that the pathogenesis of diabetic nephropathy is characterized by "internal injury and ambush of evil." This theory posits that the underlying cause of the disease lies in internal imbalances, such as stagnation of qi and blood, transformation of fire and toxins, yin and injury, and obstruction in the kidney. According to Li Peixu [10], the fundamental pathogenesis of diabetic nephropathy is attributed to deficiency of qi and yin, a condition that predominates in the early and middle stages of the disease.

2.3 Staging in Chinese Medicine

Diabetic nephropathy is characterized by a multifaceted etiology and pathogenesis, resulting in a spectrum of complex symptoms that vary in their manifestation among different medical practitioners. Professor Ni Qing [11] proposed a classification system that categorizes DKD into three stages: early, middle, and late. He theorized that the primary causative agent of DKD in the early stage is spleen qi deficiency, while in the middle stage, it is kidney qi deficiency, and in the late stage, it is kidney yang deficiency. In contrast, Prof. Chen Lixia [12] posited that early diabetic nephropathy is primarily marked by deficiency of qi and yin. Prof. Chen further theorized that DKD originates from thirst-quenching

disease, thus its fundamental etiology and pathogenesis are also characterized by deficiency of yin, with dryness and heat manifesting as the predominant symptoms. As the disease progresses, the deficiency of qi and yin causes damage to the spleen and kidney, leading to the middle stage of diabetic nephropathy. This stage is primarily characterized by deficiency of the spleen and kidney, as well as the accumulation of water and dampness, and a decline in renal function. Ultimately, this results in the development of end-stage nephropathy. Zhao Jinxi et al. [13] proposed a classification system that categorizes DN into three phases according to clinical manifestations. The early stage is designated as CKD IV1, the middle stage as CKD IV2, IV3, and V, and the late stage as CKD IV2, IV3, and V. This classification system facilitates the diagnosis and treatment of DN by distinguishing between three types of early and middle stage symptoms and twelve types of late stage symptoms.

2.4 Traditional Chinese Medicine (TCM) Internal Treatment

2.4.1 Staged Treatment

Early stage of DKD is primarily marked by a deficiency of both qi and yin, accompanied by symptoms such as dryness and heat. Professor Liu Ximing's perspective on the treatment of DKD is rooted in the belief that the replenishment of qi is accompanied by the nourishment of yin. According to Professor Liu, the loss of qi does not occur in isolation, and the nourishment of yin does not occur in isolation. He further posits that yin has the capacity to decelerate and transform qi, thereby emphasizing the notion that biochemistry is infinite [14]. Tong Xiaolin et al. [15] posited that the therapeutic approach to diabetic nephropathy is predicated on deficiency, and the treatment is aimed at replenishing deficiency and tonifying qi. Consequently, Astragalus Jianzhong Soup is employed to accentuate the essence of the disease, with flexible additions and subtractions based on the identification and typing of DN. Conversely, Prof. Wang Yaoguang subscribes to a different theoretical framework, positing that the fundamental etiology of DN is rooted in deficiency of both qi and yin. In response, Prof. Wang employs a modified version of Senqi Di Huang Tang, introducing additional modifications to the formula to target early DKD [16]. Conversely, Prof. Wu Jiachen's perspective on early diabetic nephropathy is characterized by deficiency of qi and yin, which primarily affects the spleen and kidney organs. Prof. Wu's treatment approach emphasizes tonifying the kidney as being more effective than tonifying the spleen, frequently employing Sijunzi Tang with added flavor [17].

According to the Yellow Emperor's Classic of Internal Medicine, "Yang qi is akin to the sky and the sun." This signifies that yang qi possesses the capacity to counteract external aggressors. In a study by Xu Lin et al. [18], the efficacy of insulin combined with solid spleen powder in treating DKD with spleen and kidney yang deficiency was examined. The study group exhibited a superior reduction in glucose levels and improvement in symptoms such as lack of warmth in the hands and feet and loose stools when compared to the control group treated with insulin alone. Yang Zhongqiu's research [19] examined the therapeutic efficacy of tonifying yang and restoring five soups in DN patients. The

long-term clinical trials demonstrated that patients exhibited significant improvements in 24-hour urinary proteins, validating the effectiveness of the treatment. Concurrently, a school of thought posits that the incorporation of astragalus, cinnamon, yam, dihuang, psyllium, prepared epimedium, and fried atractylodes can attenuate inflammation, fortify the kidneys, and stimulate the spleen and kidneys. Psyllium, Chinese yam, saffron, Radix et Rhizoma, Radix et Rhizoma Glycyrrhizae, Rhizoma Atractylodis Macrocephalae, Rhizoma Atractylodis Macrocephalae, and Rhizoma Atractylodis Macrocephalae have been shown to nourish the kidneys, thereby eliminating blood stasis and strengthening the kidneys to dissolve phlegm, a condition that is particularly relevant for patients with phlegm- and lung-deficiency [20].

In the advanced stage of diabetic nephropathy, the spleen and kidneys exhibit deficiencies in yang and qi, impeding their capacity to facilitate the flow of qi and blood. This results in blood stagnation and stasis, as well as an impaired ability to transport and transform water and dampness, which ultimately accumulates as dampness-heat. Lu Yangman et al.[21] observed the effect of Strengthening the Spleen and Consolidating the Kidneys and Eliminating Blood Stasis Formula on the excretion rate of urinary microalbumin, urinary microalbumin, urinary connective tissue growth factor level, and serum angiopoietin and its receptor level of diabetic nephropathy patients before and after treatment, and counted the points of traditional Chinese medicine (TCM) symptoms before and after the treatment, and found that the Strengthening the Spleen and Consolidating the Kidneys and Eliminating Blood Stasis Formula could reduce some laboratory indexes of the patients and improve the points of TCM symptoms. Yang Chenhua et al. [22] concluded that diabetic nephropathy is mainly characterized by phlegm-dampness, which can be treated with hard and warm Cangzhu, Houpu, Huo Xiang and Peilan; blood stasis can be treated with pungent and warm Safflower, Rhizoma Ligustici Chuanxiong and pungent and cool Pueraria lobata. The treatment of wind and clearing collaterals can be achieved through the use of insect medicines such as cicada metamorphosis, stiff silkworms, leeches, scorpions, and centipedes. The efficacy of medicines can be enhanced by the use of pungent medicine in cases of spleen-renal and yin- and blood-deficiency.

2.4.2 Application of proprietary Chinese medicines

Wu Jian et al [23] found that Bailing capsule and rhubarb stinging insect pill combined with Western medicine based treatment for improving proteinuria in diabetic nephropathy was better than Bailing capsule alone based on Western medicine treatment, especially for improving β 2-microglobulin, urinary microalbumin, 24h urine protein quantification in early diabetic nephropathy with good clinical efficacy. Jiang Tingting et al [24] in a clinical observational study found that the combination of Huangkui capsule capsule based on Western medicine treatment for patients with diabetic nephropathy stage III and IV can significantly promote the improvement of their vascular endothelial cell function. Li Penghui et al [25] applied eleven tastes of beneficial renal sugar-lowering tablets to treat 60 cases of early diabetic nephropathy with qi and yin deficiency and stasis type, and the overall efficacy rate of the treatment group

reached 83.3%. Xie Qiu-fang et al [26] used Cordyceps sinensis kidney tonic capsule to improve the clinical symptoms and glucose-lipid metabolism related to Chinese medicine in patients with early diabetic nephropathy, and to protect the kidneys.

2.4.3 Use of individual herbs.

Modern research has shown that astragalus and yam can lower blood sugar, reduce urinary protein excretion, lower serum urea nitrogen and creatinine levels, and also improve renal pathological damage. Wang Qin et al [27] proved that astragalus has the effect of diuresis and swelling, preventing or reversing urine protein and delaying the process of fibrosis and sclerosis of renal tissues, which has a preventive effect on the development of diabetic nephropathy. Zhang Yongxuan [28] found that in patients with diabetic nephropathy treated with Benadryl, with the addition of Astragalus injection in the observation group, the patients' urinary albumin excretion rate, urinary microalbumin, urinary β 2-microglobulin, serum TGF- β 1 and VEGF levels were significantly better than those treated with Benadryl alone in the conventional group. Ma Xiaowei et al [29] showed that the active ingredients in Radix Rehmanniae include Radix Rehmanniae methyl ester, Radix Rehmanniae lactone, and kaempferol, which can help to protect patients' kidney function, reduce urinary protein, and anti-inflammation.

2.5 External Treatment of Traditional Chinese Medicine

Relevant clinical studies have shown that the efficacy of external treatment of Chinese medicine in the treatment of diabetic nephropathy is remarkable. Acupuncture and moxibustion are used to prevent and treat diseases through the conduction effect of meridians and acupoints, as well as the application of certain manipulation methods, by stimulating acupuncture points or specific parts of the body surface to achieve the effects of warming the meridians and collaterals, dispersing cold and relieving pain, and tonifying and strengthening the body. Acupuncture therapy has its unique advantages, has a wide range of adaptability, is easy to use, economical and effective, and can reduce the economic burden of patients. Wang Man et al [30] observed 144 cases of diabetic nephropathy patients, in the treatment of diabetic nephropathy based on acupuncture therapy for intervention, the results show that the combined treatment can effectively affect the generation of inflammatory factors, improve the oxidative stress response, so as to delay kidney damage. Xie Jing et al [31] used Dan hirudinea glucose-lowering capsule combined with acupuncture treatment, and the results showed that acupuncture can improve the efficacy of hypoglycemia and reduce proteinuria, thus delaying the progression of diabetic nephropathy to end-stage. Scholars have studied that renal microvascular damage can be effectively repaired by electroacupuncture to protect the kidneys [32]. Fei Aihua [33] observed two groups of early diabetic patients, in the basic treatment with moxibustion treatment, the results showed that the treatment group urinary albumin excretion rate than the control group significant, so it shows that moxibustion in the adjuvant treatment of diabetic nephropathy has a very good therapeutic effect. Chinese herbal enema is also a common treatment for diabetic nephropathy. Chinese herbal enema is the herbal soup directly into the enema into the intestines

through the intestinal mucosa into the blood circulation, creatinine and other metabolites from the intestinal tract, thus reducing the damage to the kidneys [34]. In addition to acupuncture and herbal enemas, some studies have shown that auricular pressure beans, herbal footbaths, and acupuncture patches also have good efficacy in reducing urine protein, improving kidney function, and delaying the progression of diabetic nephropathy. Guo Xiyang [35] in the treatment of diabetic nephropathy through the observation of auricular acupressure method, taking the liver, kidney, endocrine, gallbladder, Sanjiao, pancreas, adrenal glands and other acupressure points, the results of the study showed that the treatment group of clinical symptoms and signs, the level of 24 h urinary microalbumin than the control group was significantly reduced and reduced.

3. Combination of Chinese and Western medicine

At present, the treatment of diabetic nephropathy by Western medicine is mainly by managing patients' lifestyle (such as exercise, reasonable diet, etc.), controlling blood sugar, controlling blood pressure, regulating blood lipids, etc., which is difficult to treat the disease fundamentally, and there are certain limitations and shortcomings. Some studies have shown that the clinical effect of combined Chinese and Western medicine in the treatment of diabetic nephropathy is better than that of Western medicine alone, and the combined treatment of Chinese and Western medicine can more effectively reduce urine protein and protect kidney function, so as to slow down the progress of diabetic nephropathy. In recent years, the combined treatment of diabetic nephropathy with Chinese and Western medicine has been recognized by many scholars, and on the basis of Western drugs for lowering sugar, lipid and blood pressure, combined with the analysis of the etiology of Chinese medicine as well as dialectical typing, and combined with the addition and subtraction of single-flavored traditional Chinese medicine, classical Chinese medicine prescription, proprietary Chinese medicine and Chinese medicine characteristic therapy, research has proved to have achieved a very good effect in the treatment [36]. Jiang Mei-Qiong et al. through the controlled group test, the control group taste simply with dagliflozin group, the treatment group in the dagliflozin based on the combination of xanthone capsule, the results of the study showed that the treatment group combined with xanthone capsule can effectively inhibit inflammatory response, has a good effect of lowering glucose and preserving the kidneys [37]. Huang Hai et al. observed two groups of diabetic patients with moxibustion combined with valsartan and valsartan alone, and concluded that moxibustion combined with valsartan treatment could effectively reduce the relevant indexes of patients with early diabetic nephropathy and alleviate kidney damage by comparing the levels of 24-hour urine volume, 24-hour urine protein quantification, blood urea nitrogen (BUN), blood creatinine and so on [38]. Li Xiaojian et al. found that in clinical observation, using Sijunzi Tang as the basic formula and adding drugs such as tonifying kidney qi and resolving dampness and turbidity to form Yi Kidney and Spleen Strengthening Soup for the treatment of patients with stage IV diabetic nephropathy, Chinese medicine treatment can significantly reduce the levels of urinary protein, creatinine and urea nitrogen compared with the treatment of

Western medicine alone [39]. Liu Xuqin et al [40] conducted a randomized double-blind trial of Guo Jianlin's self-formulated Jiawei Shengdi Liuwei Tang combined with Western medicine for the treatment of CKD, which showed that the blood glucose metabolism, renal function, T-cell subsets, and renal fibrosis indexes of the study group were significantly better than those of the control group, indicating that the combination of traditional Chinese and Western medicine can significantly improve renal function and slow down the progression of diabetic nephropathy.

4. Summary

Diabetic nephropathy is one of the most common and deadly complications of diabetes mellitus and has become the leading cause of death from chronic kidney disease and end-stage renal disease worldwide. Therefore, it is crucial to find effective ways to prevent and control the disease. The etiology and pathogenesis of diabetic nephropathy are complex and varied, and modern medicine has certain limitations in preventing and treating this disease. Although there are many treatment methods in Chinese medicine, there are certain limitations and deficiencies that need to be further explored and improved. Clinical workers need to further explore and learn how to combine Chinese and Western medicine to treat this disease, solve patients' pain and suffering, and improve patients' quality of life.

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