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Research Progress in Integrative Traditional Chinese and Western Medicine in Delaying the Progression of Chronic Kidney Disease

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Abstract: ***In recent years, the incidence and hospitalization rates of chronic kidney disease (CKD), especially end-stage renal disease, have risen significantly, posing a severe threat to human health. The most common etiologies are kidney diseases caused by chronic nephritis, diabetes mellitus, and hypertension, with a clear increase in CKD incidence in China. For early-stage CKD patients, reversal may be possible if the underlying cause is removed and active treatment is administered; however, patients in the middle to late stages require lifelong management to delay disease progression. Modern medicine primarily adopts a comprehensive prevention and management strategy, while traditional Chinese medicine (TCM) also plays a noteworthy role in slowing the progression of chronic kidney disease, offering the advantages of reduced adverse effects, ameliorating disease status, and decreasing relapse rates, with irreplaceable value that modern medicine cannot provide. This paper elaborates on the integrated use of Chinese and Western medicine to delay CKD progression, aiming to provide better clinical guidance for preventing the advancement of CKD to end-stage renal failure.***

Keywords: Integrative Traditional Chinese and Western Medicine, Chronic Kidney Disease (CKD), Delay in Progression.

1. Introduction

Chronic kidney disease (CKD) is defined as structural or functional abnormalities of the kidney for ≥3 months resulting from various causes, including markers of kidney damage (such as albuminuria, abnormal urinary sediment, tubular disorders, histological or imaging abnormalities) or a history of kidney transplantation, with or without decreased glomerular filtration rate (GFR); or an unexplained decrease in GFR (<60 ml/min) lasting ≥3 months. The prevalence of CKD in China is 10%–13%, making it a major disease threatening human health following cancer, cardiovascular and cerebrovascular diseases, and diabetes, and it has become a significant global public health issue. Currently, over 500 million people worldwide suffer from varying degrees of CKD. Given China's large population, the number of CKD patients is sizable, with epidemiological studies showing a prevalence rate of 10.8% among Chinese adults. Based on this rate, it is estimated that there are approximately 120 million adult CKD patients in China; without effective prevention and treatment, CKD could become a substantial social and economic burden. Traditional Chinese medicine (TCM) has unique advantages in treating CKD, helping to reduce adverse drug reactions, ameliorate disease progression, and decrease relapse rates, offering irreplaceable value compared to modern medicine. Integrative therapy combining Chinese and Western medicine can significantly improve patient symptoms, enhance quality of life, and is of great importance in delaying CKD progression.

2. The Traditional Chinese Medicine Understanding of Chronic Kidney Disease

2.1 Disease Nomenclature

There is no direct description of CKD in ancient Chinese medical literature; however, based on the common clinical presentations of CKD—such as fatigue, nausea, lumbar pain, edema, and oliguria—TCM theory considers CKD to fall within the categories of "yao tong" (lumbar pain), "xu lao" (consumptive disease), "shui zhong" (edema), "guan ge" (obstruction), and "long bi" (dysuria/urinary retention).

2.2 Etiology and Pathogenesis

Professor Chen Zhiqiang [1] believes that the primary location of this disease is the kidney, but it also involves multiple internal organs including the lung, spleen, stomach, bladder, and sanjiao (triple burner, a concept in TCM referring to functional divisions of the body). The causes of kidney disease are generally divided into two categories: those caused by heredity or gene mutation, which are considered congenital deficiency of endowment; and those resulting from improper dietary regulation, which are seen as acquired malnutrition.

With long-standing renal disease, the patient's kidney essence becomes deficient, the spleen's transport function is impaired, and the ability to transform qi (vital energy) is insufficient. Malfunctions in the opening, closing, ascending, and descending of bodily functions occur, manifesting as failure to ascend or descend, to store or release substances as needed, resulting in a syndrome of root-deficiency and manifestation-excess. Water retention may arise and overflow to the skin, causing edema, or accumulate in the chest and abdomen, leading to pleural effusion or ascites; the kidney loses its retaining function, and essential substances leak, resulting in proteinuria and hematuria; dampness accumulates into turbidity, and impaired ascending and descending functions manifest as oliguria, nausea, and vomiting. The root cause is thought to be the spleen. Kidney deficiency, combined with water-dampness and damp-turbidity, constitutes the main pathological factors. Chronic illness may lead to collateral stasis, manifesting either as stasis from deficiency or from dampness, with co-existence of water and

blood stasis or blockage of collateral vessels.

Exogenous pathogenic factors, especially wind-cold and wind-heat, are the main triggers and exacerbating factors for this disease. Exposure to such external pathogens impairs the lung wei (defensive qi), disrupts the lung's regulatory function, obstructs water metabolism, leading to an abundance of dampness and turbidity, and further depletes qi of the spleen and kidney, resulting in greater deficiency and pathogen excess.

Unhygienic (or irregular) diet impairs the spleen and stomach, disrupting their transforming and transporting functions, leading to accumulation of dampness and formation of turbidity, or dampness retaining heat, producing damp-heat.

Excessive fatigue can damage the heart and spleen, while excessive sexual activity can deplete kidney essence and injure kidney qi. Deficiency of spleen and kidney impairs transformation of qi and water, and disrupts the ascending of the clear and descending of the turbid, resulting in water retention and obstruction of dampness, ultimately leading to syndromes such as shenlao (kidney fatigue) and guange (urinary obstruction). Kidney essence deficiency can also result in poor nourishment of the liver, leading to internal stirring of liver wind.

In summary, the primary location of this disease is the kidney, but it also involves the lung, spleen (stomach), and liver. The basic pathogenesis is root-deficiency with manifestation-excess: root-deficiency mainly refers to kidney essence deficiency; manifestation-excess refers to syndromes such as water retention, damp-turbidity, damp-heat, blood stasis, and internal stirring of liver wind.

2.3 Internal Treatment Methods of Traditional Chinese Medicine

According to the Traditional Chinese Medicine (TCM) Clinical Pathway for Chronic Renal Failure issued by the National Administration of Traditional Chinese Medicine in 2017, CKD syndrome differentiation is divided into four patterns of deficiency ("zheng xu zheng xing") and four patterns of excess ("xie shi zheng xing"). Recommended prescriptions are provided based on clinical manifestations of each pattern: for spleen-kidney qi deficiency pattern (pi shen qi xu zheng), Shenling Baizhu powder (Shenling Baizhu San) and Buzhong Yiqi decoction (Buzhong Yiqi Tang) are used to tonify the spleen and kidney; for spleen-kidney yang deficiency (pi shen yang xu zheng), Zhenwu decoction (Zhenwu Tang) or Erxian decoction (Erxian Tang) are administered to warm and supplement spleen-kidney yang; for dual yin-yang deficiency (yin yang liang xu zheng), Dihuang drink (Dihuang Yin Zi) is used to nourish both yin and yang, while for liver-kidney yin deficiency (gan shen yin xu zheng), Liuwei Dihuang decoction (Liuwei Dihuang Tang) or Erzhi pill (Erzhi Wan) are applied to nourish the liver and kidney. The four excess patterns—damp-heat (shi re), blood stasis (yu xue), water retention (shui qi), and turbid dampness (shi zhuo)—are treated with Ermiao powder (Ermiao San), Taohong Siwu decoction (Taohong Siwu Tang), Wuling powder (Wuling San), and Weiling decoction (Weiling Tang) respectively.

Various medical practitioners have their own insights regarding treatment approaches. Professor Tong Shaobo believes that the treatment of chronic kidney disease (CKD) requires a combination of "Fu Zheng" (supporting vital Qi) and "Qu Xie" (eliminating pathogenic factors), utilizing tonic methods together with techniques to resolve dampness, eliminate turbidity, remove blood stasis, and invigorate the channels. The flexible combination of such methods, including the use of paired Chinese medicinal herbs ("Yao Dui"), has achieved remarkable therapeutic efficacy. Professor Nie Lifang [2] considers that CKD can be divided into two stages: the "Xu Sun" (deficiency-damage) stage and the "Guan Ge" stage (Qi obstruction and block). During the deficiency-damage period, treatment mainly focuses on "Fu Zheng Qi" (supporting healthy Qi), whereas in the Guan Ge stage, the primary approach is to rescue and treat the Spleen and Stomach in the Middle Jiao (central burner). Professor Gao Jining [3] holds that treatment should focus on supplementing deficiency, dispelling wind, and resolving blood stasis. Yam (shuyu) prescription serves as the basic formula, with emphasis on rehmannia (shanyao) to supplement deficiency. The combination of fangfeng, astragalus, and atractylodes in the Yupi Feng San formula is used to dispel wind, while Taohe Chengqi Decoction is added to resolve blood stasis. Professor Zhang Binghou [4] posits that the essential pathogenesis of CKD is a mixture of deficiency and excess ("xu shi jia za"), where deficiency refers to spleen and kidney impairment, and excess involves renal collateral stasis. The treatment combines kidney tonification with methods to clear stasis in the renal collaterals. Clearing methods are further subdivided into regulating qi ("qi fen") and regulating blood ("xue fen"): when regulating qi, diuretic and dampness-resolving agents are added; for regulating blood, blood-activating and stasis-resolving medications are incorporated, thereby achieving both symptomatic and etiological treatment. Professor Dai Xiwen [5] and Professor Zhao Jingli [6] believes that "Shi Re" (damp-heat) runs through the entire course of CKD onset and progression, often interlinking with "Yu Xue" (blood stasis), "Zhuo Xie" (turbid evil), "Shui Xie" (water retention), and "Feng Du" (wind toxin), leading to lingering and refractory disease. Therefore, the approach to clear and resolve damp-heat ("Qing Li Shi Re") should be maintained throughout the entire treatment process [7]. Considers chronic kidney disease as a syndrome of root-deficiency with manifestation-excess, and identifies the key pathogenesis as dysfunction of the triple burner (sanjiao shufu). He established a clinical treatment protocol focusing on facilitating and dredging the shaoyang and triple burner, supplemented by strengthening the spleen and benefiting the kidney, combining therapies to dispel wind and unblock collaterals, promote diuresis and remove dampness, clear heat and dry dampness, eliminate turbidity and detoxify, and invigorate blood and resolve stasis, thus addressing both root and manifestation. Professor Sun Yuzhi [8] asserts that the root of chronic kidney disease lies in deficiency of the spleen and kidney, while the manifestation is a combination of damp-heat and blood stasis, with wind pathogen being the reason for lingering disease. Therefore, clinical practice should be centered on treating the kidney, harmonizing all the zang organs, supplemented with the method of regulating the extraordinary meridians, and integrating both internal and external therapies.

2.4 External Treatment Methods of Traditional Chinese Medicine

External treatment methods of Traditional Chinese Medicine (TCM) serve as important adjuncts in the management of chronic kidney disease. These methods have a long history in China. The "Suwen • Discussion on Essential Truth" records: "For diseases located inside the body, internal medications or internal regulation methods should be used; for issues on the body surface, external application of drugs or external manipulation should be employed." The "Suwen • Discourse on Correspondence of Yin and Yang" notes: "When pathogenic evil is located within the body, decoctions and sweating therapy may be used to expel it; for superficial (external) pathogens, sweating therapy directly eliminates external evil." These suggest the use of fomentation and sweating methods for the treatment of edema [9]. Li Yue Pian Wen is a specialized ancient Chinese treatise on external therapies. It states, "The principle of external treatment is the same as internal treatment," and provides detailed records of various prescriptions and methods using external application of medicines for the treatment of edema and kidney-related diseases. For example, plasters made from yang-warming and diuretic herbs are applied to specific body sites to treat edema caused by kidney yang deficiency, embodying the holistic TCM concept that external therapy can regulate the balance of yin and yang of the zang-fu organs and improve kidney disease status. In the classic Treatise on Febrile Diseases by the Medical Sage Zhang Zhongjing, it is recorded: "Take one large pig's gallbladder, drain the bile, mix with a small amount of vinegar, administer per rectum, and after about the time of a meal's duration, stool and retained food residues will be expelled with significant effect." This pioneered the rectal administration of Chinese medicines. Although not directly targeted at renal disease, this concept has paved the way for enemas using Chinese herbs for detoxification in the treatment of kidney diseases in later generations.

2.4.1 Acupoint Application (Acupoint Plaster Therapy)

Chinese herbal preparations are ground into powder, mixed with ginger juice and other media, and then applied to specific acupoints, such as Shenshu (BL23) and Shenque (CV8). The medication is absorbed through the skin at these points, exerting actions such as warming the kidney, strengthening the spleen, promoting diuresis, and alleviating edema. For instance, in CKD patients with spleen-kidney yang deficiency, topical applications containing warming herbs like Aconite (Fuzi) and Cinnamon (Rougui) can relieve symptoms such as soreness and weakness of the lower back and knees, cold intolerance, cold limbs, and edema. In a clinical study, 60 CKD patients were randomized into an experimental group and a control group. The experimental group received acupoint patch therapy with warming yang and activating blood circulation plaster based on the control group's treatment. Selected acupoints included Qihai (CV6), Shenshu (BL23), and Zusanli (ST36). After two weeks, statistical analysis demonstrated that while improvement in renal function was not significantly different between the groups, the total effective rate for edema relief was higher in the experimental group than in the control group, with the difference being statistically significant ($P<0.05$) [10].

2.4.2 Chinese Herbal Enema

The main purpose is to eliminate toxins through the intestine. Decoctions of Chinese herbs are administered rectally, allowing the medicinal substances to exert local effects in the gut and promote the elimination of toxins. For instance, enema solutions prepared with rhubarb (dahuang) and similar drugs can effectively lower serum creatinine and blood urea nitrogen levels, thereby improving renal function in patients.

2.4.3 Chinese Herbal Bath Therapy

Patients are immersed in a bath containing Chinese medicinal ingredients. Herbs penetrate through the skin, exerting effects such as regulating meridians and promoting sweating and detoxification. In chronic kidney disease patients with pruritus, herbal baths using sophora flavescens (kushen), kochia (difuzi), etc., can relieve skin itching and facilitate the removal of internal damp-toxins.

2.4.4 Moxibustion (Moxa Therapy)

Moxibustion on acupoints such as Zusanli and Sanyinjiao can warm yang and reinforce qi. For CKD patients with qi and blood deficiency and yang deficiency, this therapy can improve overall vitality, enhance the body's resistance, and help stabilize the disease process.

3. Progress in Modern Medical Research on Chronic Kidney Disease

3.1 Overview

Chronic kidney disease (CKD) refers to kidney structural or functional abnormalities persisting for ≥3 months resulting from various causes, including markers of kidney injury (such as albuminuria, urinary sediment abnormalities, tubular disorders, histological abnormalities, and imaging abnormalities), or a history of kidney transplantation, with or without a decrease in glomerular filtration rate (GFR). A persistent decline in GFR of unknown origin (<60 ml/min) for ≥3 months also meets the diagnostic criteria. In recent years, the incidence and hospitalization rates of chronic kidney disease, especially end-stage renal disease, have markedly increased, posing a serious threat to human health. The primary etiologies of CKD include primary and secondary glomerulonephritis, diabetic nephropathy, hypertensive nephrosclerosis, tubulointerstitial disease, renovascular disease, and hereditary disorders. Among these, chronic glomerulonephritis, diabetes, and hypertension-induced renal diseases are the most common causes. With increasing prevalence of diabetes, hypertension, obesity, and an aging population in recent years, the incidence of CKD in China has also risen significantly.

3.2 Epigenetic Research on Chronic Kidney Disease

Epigenetic modification refers to changes in gene expression without alterations in the traditional DNA sequence structure. These modifications are relatively stable and can be inherited across generations. Current domestic and international research suggests that epigenetic modifications are likely to

be the molecular foundation underlying the pathogenesis and certain phenomena associated with various chronic kidney diseases. This perspective facilitates the identification of new therapeutic targets and diagnostic strategies for CKD through the lens of epigenetic modification, the investigation of targeted interventions, the prediction of disease severity, and the development of biomarkers to help assess prognosis.

The mechanisms of epigenetic modification primarily include traditional DNA methylation, post-translational histone modifications (PTHMs), and non-coding RNAs (ncRNAs). In addition, genomic imprinting, gene silencing, chromatin remodeling, chromosomal inactivation, and maternal effects are also areas of interest in epigenetics research. Both environmental factors and lifestyle can influence the epigenetic state [11]. Unlike genetic variation, epigenetic modifications are reversible, thus having tremendous value in the diagnosis and treatment of diseases.

IgA nephropathy (IgAN), the most common form of primary glomerular disease in China, is widely recognized in studies to be critically associated with galactose-deficient IgA1 (Gd-IgA1), which is a key factor in the pathogenesis of IgAN [12]. Downregulation of core 1β1,3-galactosyltransferase (C1GalT1) and its molecular chaperone (C1GalT1 molecular chaperone, Cosmc) is an important reason for the production of galactose-deficient IgA1 (Gd-IgA1); however, the underlying causes of these enzymatic abnormalities remain unclear. Current studies suggest that aberrant epigenetic regulation may be responsible [13]. Minimal change disease (MCD) is the most common type of nephrotic syndrome in children. In naïve T helper cells from patients with relapsed and remitted MCD, as well as from healthy controls, a total of 82 differentially methylated genes have been identified. The methylation levels of these genes fluctuate with disease activity and are mainly functionally associated with the tumor necrosis factor-alpha (TNF-α) or nuclear factor kappa B (NF-κB) pathways, thereby contributing to the pathogenesis of MCD [14].

Epigenetic regulation studies of chronic kidney disease will help us to better understand certain mechanisms of CKD pathogenesis and support further advancements in future treatment strategies.

3.3 Treatment

Modern medicine typically employs comprehensive preventive and therapeutic strategies to delay the progression of chronic kidney disease (CKD), including lifestyle modification and nutritional therapy, achieving target levels of urinary protein, controlling target blood pressure and blood glucose, correcting dyslipidemia, managing hyperuricemia, and preventing or treating infections. It is vital to identify and manage risk factors related to renal function deterioration, with hypertension and diabetes mellitus currently being the most prevalent causes of high global CKD incidence.

3.3.1 Hypertension

Renal lesions in CKD patients lead to a reduction in functional nephron units and a consequent decline in GFR, resulting in water and sodium retention and increased volume load. These factors are fundamental initiating and pathophysiological bases for persistent hypertension in CKD patients. Water and sodium retention and increased volume load can activate the sympathetic nervous system, stimulate juxtaglomerular cells to produce renin, and elevate levels of angiotensin II [15]. It results in the abnormal activation of the renin-angiotensin-aldosterone system (RAAS), directly causing glomerular injury, leading to ischemic glomerulosclerosis and constriction of efferent arterioles, with a consequent increase in intraglomerular pressure [16].

Regarding the treatment of hypertension in chronic kidney disease (CKD), the main pharmacological agents include ACEI/ARB (Angiotensin-Converting Enzyme Inhibitors / Angiotensin Receptor Blockers), diuretics, calcium channel blockers, and natriuretic peptides. Taking ACEI/ARB as an example, the renin-angiotensin-aldosterone system (RAAS) is a key endocrine system in the regulation of blood pressure, fluid balance, and electrolyte homeostasis in the human body. Abnormal activation of RAAS is closely associated with diseases such as hypertension, chronic kidney disease, and heart failure. Angiotensin I is converted to angiotensin II, the core active substance of RAAS, under the action of angiotensin - converting enzyme (ACE). Angiotensin - Converting Enzyme Inhibitors are cornerstone medications in the treatment of hypertension and CKD, with representative drugs including captopril and enalapril. The primary mechanisms of ACEI include inhibition of Ang II production, reduction of aldosterone release, elevation of bradykinin levels, and cardioprotective and renoprotective effects.

3.3.2 Diabetes Mellitus

SGLT2 inhibitors (sodium-glucose cotransporter-2 inhibitors) are a novel class of hypoglycemic agents, with representative drugs including empagliflozin, dapagliflozin, and canagliflozin. Although the hypoglycemic effect in CKD patients may be attenuated, SGLT2 inhibitors still provide significant renal protection through a variety of metabolic and hemodynamic mechanisms, such as improvement of intraglomerular hypertension, reduction of inflammation and fibrosis, amelioration of metabolic dysfunction, and decrease in volume overload, thus delaying CKD progression. SGLT2 inhibitors have emerged as a breakthrough therapy in CKD management, offering not only glycemic control but also independent cardiorenal protective effects.

4. Conclusion

Integrative traditional Chinese and Western medicine possesses unique advantages in delaying the progression of chronic kidney disease. It enables a more comprehensive prevention and treatment approach, reduces toxic side effects, alleviates the disease process, and decreases relapse rates in patients. In combination with diverse TCM external therapies, it addresses both the root and manifestation, improving symptoms while reducing the renal burden. The prospects of integrated TCM and Western medicine in delaying CKD progression are broad and warrant further research and exploration.

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