REVIEW ARTICLE

Study on the Progress of Application of Qingxin Lianzi Drink in Paediatric Nephrotic Syndrome

Yongzheng Zhang, MM; Lin Du, MM; Bonan Liu, MM; Hai Wang, MD

ABSTRACT

Nephrotic syndrome, a common kidney disease syndrome in children, has triggered extensive clinical research to identify safe and effective treatments. Qingxin Lianzi Drink, as a traditional Chinese medicine prescription, has been paid more and more attention in the treatment of nephrotic syndrome in children. Its main ingredients include Shilotus meat, scutellaria skullcap and ground bone skin, etc. These ingredients have the effects of clearing heat and detoxifying, reducing swelling and water, and nourishing liver and kidney. In the treatment of nephrotic syndrome in children, Qingxin Lianzi Drink can play a role in many ways: first, it can inhibit inflammatory response, reduce glomerular inflammatory damage, relieve proteinuria and other symptoms; Secondly, the ingredients such as stone lotus meat can promote the excretion of waste and water in the body, reduce edema and edema and other symptoms; Finally, scutellaria and other ingredients can nourish liver and kidney and promote the recovery of liver and kidney function. At present, a large number of studies have found that Qingxin Lianzi Drink has obvious effect on chronic kidney disease. In addition, Qingxin Lianzi Drink as a natural therapy, compared with traditional western medicine treatment, more safe, natural and effective, has been widely concerned. Therefore, Qingxin Lianzi Drink in the treatment of children with nephrotic syndrome of the mechanism of action and efficacy evaluation of the study is of great significance. In this paper, combining the pathogenesis and treatment status of nephrotic syndrome in children, the mechanism of Qingxin Lianzi Drink in the treatment of nephrotic syndrome is explored, which can better understand its effectiveness in the treatment of nephrotic syndrome in children, and provide scientific basis for its application in clinical practice. (*Altern Ther Health Med.* 2023;29(8):882-891).

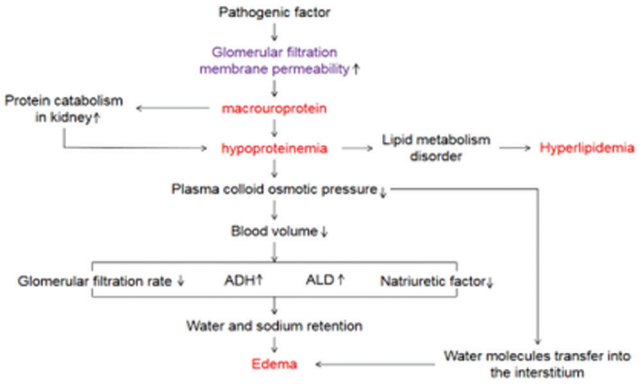
Yongzheng Zhang, MM; Bonan Liu, MM; Hai Wang, MD; The Second Department of Pediatrics, the First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, People's Republic of China. **Lin Du, MM; T**he Fourth Department of Cardiology, the First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, People's Republic of China.

Corresponding author: Hai Wang, MD
E-mail: zhyzh2016@163.com

INTRODUCTION

Nephrotic syndrome, characterized by obvious proteinuria, hypoproteinemia, edema and hyperlipidemia, is a common urinary system disease in children. The disease usually strikes in children between the ages of 2 and 6 and is more common in boys than girls. The main pathogenesis involves dysfunction of normal charge and molecular barrier of renal filtration membrane. This results in increased glomerular permeability to plasma proteins and a large loss of protein in the urine that exceeds tolerance limits, leading to a range of symptoms[1] (Figure 1). But the exact cause of nephrotic syndrome in children is unknown and may involve immune system abnormalities, as well as underlying genetic and environmental factors. Certain genetic and environmental factors may also increase the risk of the disease. According to epidemiological data, nephrotic syndrome in children occurs globally, but the prevalence is higher in certain regions. The study found that the annual prevalence varied between 0.012 % and 0.035 % in children in Western Europe and up to 0.065 % in Japan.[2] The World Health Organization reports that globally, there are 20 000 to 35 000 new cases of nephrotic syndrome in children each year, with a prevalence of about 15-20 cases per 100 000 people in developed countries.[3] However, the actual prevalence may be higher than the reported figures due to difficulties in diagnosing and reporting the disease. Childhood nephrotic syndrome can significantly impact the child and his or her family. The disease may lead to edema, particularly in the face, hands, feet and abdomen.

Figure 1. Pathogenesis of pediatric nephrotic syndrome



Proteinuria and hypoproteinaemia may lead to reduced immune function and increased risk of infection. In contrast, hyperlipidemia may increase the risk of cardiovascular disease in the child, which also has a serious impact on the child's health. There are many clinical treatments for this disease, usually including medication and nutritional support. Hormone therapy is a common treatment to reduce symptoms and decrease proteinuria, while other medications such as immunosuppressants may also be used for treatment. But it is persistent and recurrent, and long-term monotherapy can lead to increased blood glucose and lipids, osteoporosis and poor growth.[4] And, because children with nephrotic syndrome are young and often immunocompromised, they are highly susceptible to poor prognosis and even death. Although more than 85% of children with nephrotic syndrome respond to corticosteroids, about 10-15% remain unresponsive or later become steroid resistant.[5] Studies have found that steroid-resistant nephrotic syndrome has a negative impact on kidney prognosis, with 36-50% of patients progressing to end-stage renal disease within 10 years.[6] Meanwhile, in the case of nephrotic syndrome in children, the impact on children and families is multifaceted. For children, nephrotic syndrome not only leads to long-term health problems but also limits their daily activities, school participation, and physical development, and even negatively affects psychosocial interaction. At the same time, nephrotic syndrome places a considerable burden on families. Families must cope with financial pressures, medical expenses, and the challenges of extra attention, care, and scheduling with their children. Therefore, seeking a safer and more effective treatment option is important for the child's recovery and quality of life. At the same time, in recent years, with the continuous development of Chinese medicine, the clinical application of traditional Chinese medicine has become a hot topic of current research.

In the field of traditional Chinese medicine, children nephrotic syndrome belongs to "edema", "exhaustion" and other categories, mainly by the spleen, kidney, lung function impairment, or both external evil invasion, resulting in the body water transport obstacles, water flooding, causing head, face, limbs and even the whole body edema. Qingxin Lianzi Drink is a traditional Chinese medicine formula, which has the effect of clearing the heart and nourishing Yin, clearing the heart fire, communicating the heart and kidney, supplementing the Qingxin Lianzi Drink, and stopping the cloudiness. It is used to treat white urine turbidness, astringent bleeding, red stool such as blood, five drenching, tiredness and thirst. This formula is from "Taiping Huimin Hodong Bureau Formula" and consists of 9 herbs. Qingxin Lianzi Drink is widely used clinically, especially for chronic urinary tract diseases, and also has significant therapeutic effects in neurasthenia, stomatitis, and diabetic nephropathy.[7-8] In children with nephrotic syndrome, due to the damage of glomerular filtration membrane, urine protein and other symptoms appear, but also produce edema, hypertension and other discomfort. Therefore, the treatment of pediatric nephrotic syndrome usually includes improving kidney function and reducing symptoms such as proteinuria and edema. The medicinal materials contained in Qingxin Lianzi Drink have the functions of promoting urination, nourishing liver and kidney, inhibiting inflammation, etc., so it has certain application value in the treatment of nephrotic syndrome in children. At the same time, in previous clinical studies,[9] it was found that Qingxin Lianzi Drink in the treatment of renal diseases has achieved obvious curative effect. A number of scholars have studied the mechanism of Qingxin Lianzi Drink components in the treatment of renal diseases, and found that it plays an important role in improving the total plasma protein of patients.[10] At the same time, Shilotus meat in Qingxin Lianzi Drink can increase the clearance ability of kidney excretion for protein, thereby reducing urine protein.[11] The flesh and scutellaria in the formula can also regulate the level of inflammatory mediators, thus playing a therapeutic role.[12] In order to clarify the application of Qingxin Lianzi Decoction in children with nephrotic syndrome, this article reviews the pathogenesis of pediatric nephrotic syndrome, the understanding and treatment of TCM on pediatric nephrotic syndrome, and the effect of Qingxin Lianzi Decoction on renal function, aiming to provide a certain reference for clinical research on pediatric nephrotic syndrome.

Pathogenesis of pediatric nephrotic syndrome

Previous studies have shown that the main pathogenesis of the pediatric nephrotic syndrome is T-cell dysfunction and/or abnormal secretion of certain circulating glomerular permeability factors.[13] Recent studies have shown that its pathogenesis is also associated with B-cell dysfunction.[14] However, the role of T-cell and B-cell dysfunction in different hormonal responses and pathological types and the specific mechanisms involved are not yet clear. Therefore, an in-depth study of the etiology and pathogenesis of the paediatric nephrotic syndrome is of great clinical importance to identify new targets for intervention to delay the chronic progression of renal damage.

Pathogenesis of nephrotic syndrome - impaired podocyte and glomerular filtration barrier

The glomerular filtration barrier is the most important pathophysiological basis for developing nephrotic syndrome, in which the podocytes are terminally differentiated cells that

are difficult to regenerate after apoptosis. Trautmann A et al.[15] found that abnormalities in the podocytes, due to various causes, contribute to the development of nephrotic syndrome. Kopp JB et al.[16] showed that the development of congenital nephrotic syndrome and some hormone-resistant nephrotic syndromes is associated with mutations in the podocyte actin backbone gene, which affects glomerular The gene mutation would affect glomerular filtration barrier function. However, the exact mechanism of podocyte damage and recovery of podocyte structure and function from glucocorticoid treatment is not known, but immune factors are recognized as the most important influencing factor.

Pathogenesis of nephrotic syndrome - immune dysfunction

It is now accepted that triggers such as vaccine infection or allergens stimulate the immune response of antigen-presenting cells (APCs) and B cells, which in turn mediate the disruption of the T-cell immune response through antigen presentation and production of cellular mediators, which in turn secrete or promote the secretion of circulating factors that target the glomerular filtration barrier, resulting in the production of large amounts of proteinuria. These factors target the glomerular filtration barrier, producing large amounts of proteinuria, a process that primarily involves T-cell and B-cell dysfunction.[17] In the acute phase of nephrotic syndrome, CD4+ T cells are reduced, and the CD4+/CD8+ cell ratio is decreased, but some studies have found no significant changes between CD4+ and CD8+ cell subsets. In adriamycin nephropathy mice, clearance of CD4+ T cells resulted in increased renal damage, suggesting that CD4+ T cells can exert a renal protective effect.[18] Studies have found that the expression of the Th2 cell-specific cytokine interleukin (IL)-13 is significantly increased in patients with nephrotic syndrome. Meanwhile, in studies related to circulating cytokine dosage interventions, in vitro stimulation, and immunosuppressive therapy in patients with nephrotic syndrome, it was found that there was an overlap in the production of Thl-like and Th2-like cytokines in patients, which suggests the presence of Th1/Th2 cell dysfunction in nephrotic syndrome. However, the Th1/Th2 cell imbalance theory cannot fully explain the process of nephrotic syndrome.[19]

In addition, the most important evidence supporting the involvement of B cells in pathogenesis comes from the therapeutic role of rituximab (Rituximab, RTX) in nephrotic syndrome. RTX is a human-mouse chimeric monoclonal antibody against pro-B cell and matures B cell surface antigens that mediates apoptosis of this subset of B cells by recognizing CD20 with high affinity.[20] In patients with reduced hormone dependency, and frequent recurrent nephrotic syndrome, where hormone use to maintain disease stability plays an important role, and RTX is not nephrotoxic and well tolerated, it may be considered an important treatment option for nephrotic syndrome. The novel CD20 antibody Ofatumumab, a fully humanized CD20 monoclonal antibody with greater affinity for CD20, was able to reduce proteinuria and improve renal function in RTX-resistant idiopathic nephrotic syndrome despite Ofatumumab.[21] This result suggests that Ofatumab is more effective than RTX in treating idiopathic nephrotic syndrome, but further validation of the findings is needed.

Pathogenesis of nephrotic syndrome - Genetic factors

Human Leukocyte Antigen (HLA) -DQA1 (SNP rs2187668) gene locus and nephrotic syndrome. The Human leukocyte antigen (HLA) -DQA1 (SNP rs2187668) locus was found to be strongly associated with the development of membranous nephropathy in European Caucasians and in Chinese patients with nephrotic syndrome.[22] Nephrotic syndrome has been found to be familially inherited, and yellow populations are more susceptible to nephrotic syndrome than white populations; the HLA-DQA1 gene is predictive of nephrotic syndrome.[23] Single nucleotide polymorphisms in HLA-DQA1 and HLA-DQB1 are strongly associated with nephrotic syndrome. However, these loci explain only a small proportion of the genetic risk for Steroid Sensitive Nephritic Syndrome (SSNS). Outside of the HLA gene system, the calcium homeostasis regulator family member 6 gene (CALHM6) has also been found to be possibly associated with SSNS.[24]

1.3.2 Single gene mutation and nephrotic syndrome

More than 70 single genes have been reported to be associated with nephrotic syndrome, while new pathogenic single genes continue to be reported each year.[25] Early identification of the genetic causes of nephrotic syndrome can help to identify early treatment strategies to discontinue immunosuppressive drugs, assist in renal transplant management and provide a basis for prenatal counseling. For example, mitochondrial mutations resulting in a deficiency of coenzyme Q10 biosynthesis occur in 1% of cases of nephrotic syndrome, and supplementation with coenzyme Q10 is effective in treating mitochondrial pleocytosis. Single gene mutations cause SRNS, implying a low risk of recurrence after transplantation. However, there are rare recurrent cases where a network of anti-nephrin antibodies is found in patients with mutations in the NPHSI (encoding the nephrin protein) gene. Single gene positivity has been found to decrease with age in children with SRNS. Mutations in foot cell genes (e.g. NPHS1, NPHS2, LAMB2 or WT1) explained 69%-85% of cases of nephrotic syndrome presenting within the first 3 months of life and 50%-66% of nephrotic syndrome between 4 and 12 months. In patients aged 1 to 6 years,the genetic component of nephrotic syndrome decreases to 25% in children, 18% in 7-12 years, and 11% in 13-18 years(Table 1).[26]

Table 1. Onset time and probability of single gene mutation in nephrotic syndrome

Nephrotic syndrome	Single gene mutation				
Onset time	Within 3 months of birth	4~12 months	1~ 6 years old	7~12 years old	13~18 years old
Incidence probability	69%-85%	50%-66%	25%	18%	11%

The pathogenesis of nephrotic syndrome - capillary wall permeability

In pediatric nephrotic syndrome, increased capillary wall permeability is one of the key factors leading to proteinuria. Under normal conditions, the glomerular capillary wall consists of three layers of endothelial cells, basement membrane, and podocytes, which can effectively prevent the leakage of macromolecules (such as proteins) from the blood into the urine. However, in pediatric nephrotic syndrome, this barrier function is impaired for a number of reasons, including the deposition of immune complexes the release of inflammatory mediators and cytokines, which in turn increases the permeability of the capillary wall. With the increased permeability of the capillary wall, proteins in the plasma can leak through the capillary wall into the renal tubular system and eventually be excreted to form proteinuria.[27] Proteinuria is one of the main manifestations of pediatric nephrotic syndrome, and its severity can be assessed based on the amount of protein in the urine. Proteinuria can cause symptoms such as oedema and hypoproteinemia, so restoring the capillary wall's normal barrier function is crucial for treating paediatric nephrotic syndrome.

Based on the above studies, it can be found that the damage of podocyte and glomerular filtration barrier, immune dysfunction, genetic factors and capillary wall permeability changes all lead to the occurrence of nephrotic syndrome in children to a certain extent. Therefore, effective intervention in these pathogenesis will improve the therapeutic effect of patients. However, the current clinical treatment of the disease is still not comprehensive, the therapeutic effect is still not ideal, and in China's traditional medicine has been the treatment of children with nephrotic syndrome related records, therefore, in-depth exploration of the treatment mechanism of traditional Chinese medicine, will provide a certain reference for the treatment of such children.

UNDERSTANDING AND TREATMENT OF PEDIATRIC NEPHROTIC SYNDROME IN CHINESE MEDICINE

Overview of pediatric nephrotic syndrome in Chinese medicine

Clinical manifestations and syndromes of nephrotic syndrome in children. Although there is no name of "nephrotic syndrome" in Chinese medicine, the clinical manifestations of this disease are mainly edema, fatigue, low back pain, heavy limb acid, nausea, and even chest tightness, asthma, abdominal distension and other diseases. The clinical manifestation is the syndrome of deficiency of Yin and Yang qi and blood, especially the deficiency of Yang qi as the root of the disease, wind evil, water dampness, damp-heat, sore poison, blood stasis and so on. The disease is located in lung, spleen and kidney, mainly in spleen and stomach. Meanwhile, The syndrome characteristics of patients mainly include kidney-yang deficiency syndrome (manifested as water-liquid metabolism disorder, waist and knees sour and soft, fear of cold and cold, frequent urination, tongue light and white, etc.), kidney-yin deficiency syndrome (manifested as water-liquid metabolism disorder, waist and knees sour and soft, night sweat enspermia, dry mouth and thirst, urine red and stool dry, tongue red and less fluid, etc.), and spleen-kidney deficiency syndrome (manifested as digestive function weakening, appetite loss, abdominal distension and loose stool, and limb fatigue Force, edema, etc.), damp-heat intrinsic syndrome (manifested as yellow urine, thirst and cold drinks, sticky stool, swollen face, etc.) four types, according to its clinical manifestations and syndromic characteristics, should belong to the Chinese medicine "edema", "vacuous fatigue" and other categories.

TCM pathogenesis of nephrotic syndrome in children. Traditional Chinese medicine believes that the pathogenesis of pediatric nephrotic syndrome mainly involves the following aspects: (1) Kidney deficiency: deficiency of kidney qi and essence is a common pathogenesis in pediatric nephrotic syndrome. As the kidneys govern water and control yin and yang, insufficient kidney qi cannot regulate water metabolism, leading to fluid retention and edema formation. (2) Blood stasis: Pediatric nephrotic syndrome patients often have both kidney deficiency and blood stasis, which can easily lead to local necrosis and exacerbate renal dysfunction. Blood stasis can also cause microcirculation disorders, affecting the glomerular filtration function. (3) Dampness obstruction: External dampness pathogens and improper diet can generate internal dampness, impeding the circulation of qi and blood and causing phlegm turbidity, which blocks the kidney meridian and leads to pediatric nephrotic syndrome. (4) Spleen-stomach disharmony: The spleen governs the transformation and transportation of water and dampness. If the function of the spleen and stomach is impaired, water and dampness will stagnate, leading to edema formation. At the same time, the poor absorption and utilization of nutrients caused by spleen-stomach disharmony will exacerbate the disease under the background of impaired glomerular filtration function. (5) Emotional disorders: Emotional factors are also one of the important causes of pediatric nephrotic syndrome, such as excessive contemplation, depression, sadness, etc., which can lead to liver qi stagnation, affecting the smooth flow of qi and blood, and ultimately causing pediatric nephrotic syndrome.

Principles of TCM treatment of nephrotic syndrome in children. The treatment principles in traditional Chinese medicine for nephrotic syndrome in children mainly include the following: (1) the interaction between the liver and kidney: there is a close relationship between the liver and kidney, and factors such as emotional disorders and Qi stagnation and blood stasis can affect the interaction between the liver and kidney during the pathogenesis of nephrotic syndrome. Therefore, the main focus of treatment should be on soothing the liver, regulating emotions, and enhancing the interaction between the liver and kidney. (2) Tonifying the kidney yang: renal yang deficiency is an important pathological mechanism in the treatment of nephrotic syndrome in children. Therefore, the main focus of treatment should be on warming and tonifying the kidney yang,

consolidating the essence and Qi, enhancing the renal function and improving the body's immunity. (3) Promoting the transformation of body fluids: patients with nephrotic syndrome in children often have symptoms of insufficient body fluids and internal water retention, which can affect the normal function of the kidneys. Therefore, the main focus of treatment should be on nourishing yin and moistening dryness, promoting diuresis and relieving swelling, and promoting the metabolism of body fluids. (4) Adjusting nutritional balance: Patients with nephrotic syndrome in children often have problems of dampness and stagnation in the spleen and stomach, and poor nutrient absorption, which can lead to decreased resistance of the body. Therefore, the main focus of treatment should be on adjusting the diet structure, enhancing the function of the spleen and stomach, and promoting the absorption and utilization of nutrients in the body. (5) Tailoring treatment to individual differences: The causes and conditions of each patient with nephrotic syndrome in children are different, so personalized treatment plans should be formulated according to their specific conditions to achieve the best treatment outcomes.

Chinese medicine treatment for pediatric nephrotic syndrome

The treatment of nephrotic syndrome in Chinese medicine begins with establishing the basic treatment for the deficiency of the spleen and kidneys and the main pathological products of the disease, such as water-dampness and blood stasis, i.e. warming the spleen and kidneys (benefiting Qi and warming Yang), resolving dampness and water, and invigorating blood stasis. At the same time, according to the different stages of the development of nephrotic syndrome or the different changes in the course of the progression of the disease, the principle of "treating the symptoms when it is urgent, and treating the root cause when it is slow" should be used to identify and treat the symptoms. If there is an external sensation, we should identify wind-cold and wind-heat and focus on dispersing wind-cold or dispersing wind-heat; if there is heat and toxicity, we should focus on clearing heat and detoxifying toxins; if there is internal congestion of damp-heat, we should focus on clearing heat and relieving dampness; if there is liver-kidney-yin deficiency or yin-deficiency and hyperactivity, we should focus on nourishing the liver and kidney or nourishing yin and submerging yang.

Combined internal and external Chinese medicine treatment. (1) Thunder fire moxibustion combined with warming spleen kidney formula Chen Fucong et al[28] selected 86 patients with primary nephrotic syndrome with spleen-kidney Yang deficiency syndrome to analyze the effects of thunder-fire moxibustion combined with warm tonifying spleen and kidney on the level of serum glucocorticoid receptor. The levels of glucocorticoid receptor-α and human blood albumin were higher than those of the control group, and the 24h urine protein quantification was lower than that of the control group after treatment. The combination of thunder fire moxibustion and warming of the spleen and kidney method was effective in treating primary nephrotic syndrome with spleen and kidney yang deficiency, improving patients' TCM symptoms, regulating glucocorticoid receptor levels, increasing patients' sensitivity to treatment, and promoting the recovery of kidney function and alleviating the disease.

(2) Jianpi Gushen prescription combined with warm acupuncture. Wang Yonggang[29] In the treatment results of 111 patients with diabetic nephrotic syndrome with spleen and kidney deficiency, it was found that the study group treated with the Spleen and Kidney Strengthening Formula combined with warm acupuncture had an overall treatment efficiency of 92.86%, which was significantly higher than that of the control group treated with conventional western medicine. At the same time, the renal function and fibrosis indexes of all patients were observed. It was found that the albumin (Alb) level in the study group was higher than that in the control group. In contrast, the blood creatinine (Scr), urea nitrogen (BUN), collagen type IV (CIV) and connective tissue growth factor (CTGF) levels were lower than those in the control group. The combination of warm acupuncture and moxibustion was effective in treating diabetic nephrotic syndrome patients with spleen and kidney deficiency, relieving clinical symptoms, promoting improvement of renal function, and inhibiting the progression of fibrosis.

Combined Chinese and Western medicine treatment. (1) Huoxue Lishui Decoction combined with prednisone. In the treatment of pediatric nephrotic syndrome, Chinese and Western medicine often use hormones and immunosuppressants as the main treatment, but with the in-depth research of Chinese medicine in the field of nephropathy treatment, the combined treatment of Chinese and Western medicine has been widely used. Chinese medicine focuses on regulating the balance of yin and yang in the whole body and improving the body's self-healing ability, which provides a useful supplement and complement to Western medicine treatment and makes the treatment effect more obvious. Guo Zhijie et al.[30] analyzed the therapeutic effect of combining Western medicine with Blood-vitalizing and Water-relieving Tang on patients with primary nephrotic syndrome. 82 patients were divided into a control group and an observation group using randomized grouping, in which the control group was treated with oral prednisone, and the observation group was treated with Blood-vitalizing and Water-relieving Tang (5 g of sandy nut, 10 g of sangzhi, 15 g each of jiao bai zhu, jin cherry, gorgonian, raspberry and dilong, 20 g each of yi mu cao, maidenhair, zelan, sumac, and lobelia) on top of that. After continuous treatment for 8 weeks, the total effective rate of treatment in the observation group was 95.12%, which was significantly higher than that in the control group (75.61%). At the same time, the creatinine, cholesterol, and urine protein quantification and plasma albumin levels of the patients in the observation group were significantly improved compared with those in the control group. This fully demonstrates that the combination of blood-vitalizing and

water-relieving soup with Western medicine is effective in the treatment of nephrotic syndrome, which can improve the renal function index and help stabilize the condition.

(2) Shenqi Dihuang Decoction plus minus combined with prednisone

Gao Rui et al.[31] investigated the efficacy of Ginseng-Qi Dihuang Tang plus and minus in treating nephrotic syndrome with Qi and Yin deficiency and the effects on serum immunoglobulins and complement in two groups, randomly divided into two groups for 12 weeks. The levels of 24-h urine protein, blood creatinine, and urea nitrogen were lower than those of the control group, the glomerular filtration rate was higher than that of the control group, the levels of serum immunoglobulin M, immunoglobulin G, complement C3 and complement C4 were higher than those of the control group, the levels of IgA were lower than those of the control group, and the overall clinical efficiency was higher than that of the control group, and the overall incidence of adverse reactions was not significantly different between the two groups. The clinical efficacy of Ginseng-Qi Dihuang Tang with addition and subtraction in the treatment of nephrotic syndrome with Qi and Yin deficiency is confirmed, and it can regulate the immune level of the body without increasing adverse reactions and has a better safety profile.Chen Qiang et al[32] selected 83 patients with proteinuria in nephrotic syndrome for study and randomly divided them into the control group (conventional drug treatment in Western medicine) and the research group (self-proposed treatment of clearing heat, eliminating blood stasis and tonifying the kidneys), and after the intervention, it was found that patients in the research group had a more obvious improvement in the improvement of clinical symptoms and were able to effectively reduce the proteinuria level of the patients in the 24-h period, restore renal function, and have a higher degree of safety.

Challenges and further research

However, there are relatively few clinical studies and evidence on the combination of Chinese and Western medicine in the treatment of pediatric nephrotic syndrome, and more high-quality studies are needed to verify the effectiveness and safety of the combination of Chinese and Western medicine in the treatment of the pediatric nephrotic syndrome. At the same time, each patient's condition and constitution are different, which requires an individualized treatment plan according to the specific situation in the clinical treatment process. Moreover, there is no clear standard treatment guideline to guide the treatment of pediatric nephrotic syndrome by combining Chinese and Western medicines, and the treatment plan is mostly adjusted according to the doctors' experience and the patients' response in the treatment process. Therefore, although the combination of Chinese and Western medicine can be useful in the treatment of pediatric nephrotic syndrome, there are still some potential challenges to be faced, and further research and professional clinical practice will help to better understand the effectiveness and feasibility of the combination of Chinese and Western medicine in the treatment of the pediatric nephrotic syndrome.

Several studies have suggested that TCM treatments, such as herbal medicine, acupuncture, tuina massage, and qigong, may promote the body's ability to heal itself by adjusting the balance of yin and yang throughout the body.[33] These methods are believed to adjust the body's physiological functions, promote blood circulation, and regulate the immune system, thereby improving overall health. However, there is still a lack of large-scale, randomized controlled clinical studies in this area to confirm the effectiveness of TCM in regulating the balance of yin and yang in the whole body and improving the organism's self-healing ability. In addition, the research has some methodological challenges, such as the lack of uniform assessment criteria and concepts that are difficult to quantify.

THE EFFECT OF QINGXIN LIANZI DRINK ON RENAL FUNCTION

Effects of the main ingredients of Qingxin Lianzi Drink on renal function.

Qingxin Lianzi Drink is a traditional Chinese medicine drink whose main ingredients include Scutellaria baicalensis, Ophiopogon (removed from the heart), Dictyostelium, Plantago asiatica, Glycyrrhiza glabra (roasted), Silybum marianum (removed from the heart), Poria cocos, Jatropha curcas (roasted with honey), and Ginseng, etc. These natural plant ingredients are believed to have antioxidant and anti-inflammatory properties and protect renal function. These natural botanicals are believed to have antioxidant, anti-inflammatory, and protective properties for kidney function. An experimental study on an animal model found that Qingxin Lianzi Drink was able to reduce kidney damage and improve kidney function. This study suggests that Qingxin Lianzi Drink exerts its protective effects by reducing inflammatory responses, regulating renal tubular function, and inhibiting oxidative stress. In addition, some clinical observational studies have also shown that Qingxin Lianzi Drink can reduce the urinary protein level, improve the glomerular filtration rate, and reduce the content of renal injury markers in urine in patients with renal diseases.[34] These results imply that Qingxin Lianzi Drink may have some potential in treating and preventing kidney diseases.

Effects of stone lotus meat on renal function and its mechanism of action. Stone lotus meat is a traditional Chinese herbal medicine which is commonly used in traditional Chinese medicine to treat kidney-related diseases. Stone lotus meat is rich in a variety of active ingredients, which have the effects of clearing heat and removing toxins, diuretic and diuretics, and are considered to have a certain protective effect on kidney function.

(1) Anti-inflammatory effects of flavonoids in the meat of stone lotus. Relevant studies have found that the main chemically active components of stone lotus meat are flavonoids (rock lotus flavonoids, stone lotus flavonoids,

rehmannosides, etc.), which have anti-inflammatory, antibacterial, and antioxidant effects and can reduce inflammatory reactions caused by urinary tract infections to a certain extent, and thus protect renal tissues from damage.[35]

(2) The diuretic effect of alkaloids in the flesh of stone lotus. Meanwhile, Fang Yiwei et al[36] similarly found that stilbene alkaloids and lotus alkaloids in stilbene meat have diuretic and diuretic effects, which can produce stimulation the urinary function of the kidneys, which in turn helps to remove waste and toxins in the body, thus serving to reduce the burden on the kidneys. Free radicals are highly reactive molecules that are unstable and react easily with other molecules in the body, leading to oxidative stress. Prolonged oxidative stress can cause damage to cells and tissues, including kidney tissues. In addition, oxidative stress may lead to inflammatory responses, fibrosis, and vascular damage, which are closely related to the development of renal failure.

(3) Antioxidant effects of polyphenols in the meat of stone lotus. Recently, Xia Yue et al[37] found that the polyphenolic compounds in stone lotus meat have antioxidant activity, and by reducing the effects of oxidative stress, the antioxidant effect of stone lotus meat can help to maintain the health of renal tissues and prevent the development of renal failure, and at the same time, the antioxidant effect can help to reduce the production of free radicals and neutralize those that have already been generated, thus reducing the damage of oxidative stress on the kidneys.

Effects of Scutellaria baicalensis on renal function and its mechanism of action. Scutellaria baicalensis is a commonly used traditional Chinese medicine with heat-clearing, detoxification, anti-inflammatory, and antibacterial effects.

(1) Baicalin in scutellaria reduced inflammation. Relevant studies have found that baicalin (Figure 2), the main active ingredient in Scutellaria baicalensis, has obvious anti-inflammatory effects. Inflammation plays an important role in kidney injury, and baicalin can inhibit the release of inflammation-related mediators such as tumor necrosis factor-α (TNF-α) and interleukin (IL)-1β, thereby reducing the inflammatory response and, at the same time, it is able to regulate the activity and interaction of immune cells and reduce the damage to the kidney caused by excessive immune responses.

(2) Baicalin in scutellaria scutellaria inhibited renal interstitial fibrosis. Wang H et al[38] found in their study that baicalin was able to reduce the levels of extracellular matrix (ECM) and inflammatory factor expression in fibroblasts by inhibiting TGF-β/Smad pathway activity, thereby inhibiting fibrosis and inflammatory responses and improving renal interstitial fibrosis to some extent in mice with unilateral ureteral obstruction.

(3) Baicalin in scutellaria baicalensis improved the pathological status of kidney tissue. Recently, Ning X et al,[39] in a study exploring the effects of baicalein on membranoproliferative glomerulonephritis and its underlying mechanisms, found that baicalein treatment also improved the pathology of renal tissues and reduced the occurrence of apoptosis, and was associated with a significant increase in the reduction of 24-hour urinary protein, serum BUN, SCr, triglycerides (TG), total cholesterol (TC), IL-1α, IL-2, IL-10 and Tet-off system regulating human interferon-gamma (IFN-γ) levels has an important role.

Figure 2. Molecular structure formula of baicalin

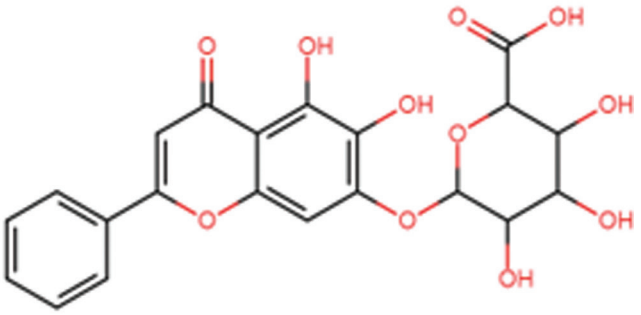
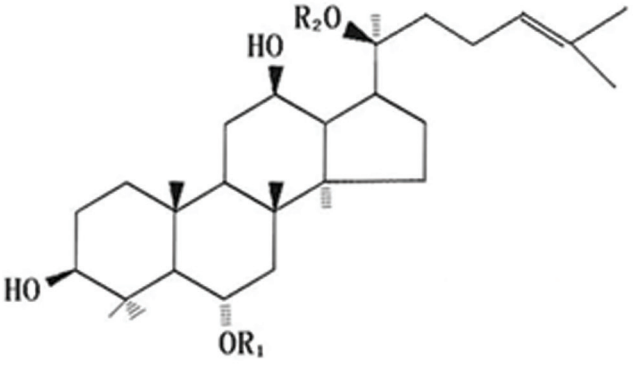


Figure 3. Molecular structure formula of ginsenoside (Rg1)



Effects of ginseng on renal function and its mechanism of action. Modern pharmacology has found that ginsenosides, the active components of ginseng, have important roles in anti-inflammation and renal protection.[40]

(1) Ginsenoside Rg1 improves cell viability and maintains mitochondrial function. Previously, Guo J et al[41] found that ginsenoside Rg1 (Figure 3) was able to reduce iron accumulation and lipid peroxidation in the process of iron death by increasing the viability of renal tubular epithelial cells, which in turn attenuated acute kidney injury to a certain extent.

(2) Ginsenosides inhibited renal fibrosis and inflammation/ Meanwhile, Zhou Q et al[42] found that the expression of adenylate-activated protein kinase (AMPK) α1 was significantly up-regulated in renal epithelial cells pretreated with Rg1, while their oxidative stress was significantly inhibited, a process that could maintain mitochondrial function, improve energy metabolism, reduce apoptosis, and ultimately protect renal tissues from acute renal ischemia-reperfusion injury. In addition, Zhang Shengxian et al[43] indicated in their study that ginsenosides in ginseng can inhibit the process of renal fibrosis, reduce the degree of connective tissue proliferation and fibrosis, and protect renal function; moreover, ginseng also contains

flavonoids, which are able to play a synergistic role with shilajit meat in inhibiting the onset and development of inflammatory responses in the kidney.

Effects of Dioscorea alba on renal function and its mechanism of action. Ground elder bark is a commonly used Chinese herbal medicine widely used in traditional Chinese medicine to treat various diseases.

(1) Antioxidant and anti-inflammatory effects of polyphenols. Relevant studies have found that the polyphenolic compounds contained in Dijian Bone Skin have significant antioxidant activity, which can neutralize the production of free radicals and reduce the damage caused by oxidative stress to the kidney. Moreover, Wei Haifeng et al[44] also showed that polyphenolic compounds (tannins) in Dioscorea can interfere with the activity of important inflammatory signaling pathways such as nuclear factor-kB (NF-kB), c-Jun N-terminally activated protein kinase (JNK) or mitochondrial pathway, and thus effectively reduce the degree of inflammation and damage in the kidneys.

(2) Anti-inflammatory effects of flavonoids. Meanwhile, Yuan Yuan et al[45] found that flavonoids (e.g., chuanxiongxizine, geraniol, etc.) in diclofenac could inhibit the production and release of inflammatory mediators (e.g., tumor necrosis factor-alpha, etc.), thus reducing inflammatory responses in renal tissues.

Qingxin Lianzi Drink in the treatment of nephrotic syndrome

Zhang Yongzheng et al[46] in order to explore the curative effect of modified Qingxin Lianzi Drink on adriamycin nephrotic syndrome rats and its effects on urinary protein, blood biochemical indexes and inflammatory mediators, used tail vein injection of adriamycin to establish a model of nephrotic syndrome in rats, which was treated by gavage treatment of model rats with Qingxin Lianzi Drink. It was found that, after the administration of the drug, the serum 24h urinary protein levels, IL-1β, IL-8, TNF-a, monocyte chemotactic protein-1 (MCP-1), TG, TC, BUN, Scr levels were reduced. The ALB The levels of ALB, plasma total protein (TP) were significantly increased. It suggests that Qingxin Lianzi Drink can reduce the urinary protein of rats with nephrotic syndrome, improve their blood biochemical indexes, and participate in regulating the expression of inflammatory mediators, which is able to improve the pathological damage, restore the functions of lung, spleen, and kidney, and play a therapeutic role in nephrotic syndrome. At the same time, long-term use of hormones will cause some adverse reactions, the use of Chinese medicine plus the flavour Qingxin Lianzi Drink can improve the safety of patient treatment in the treatment of mild nephrotic syndrome can be used as a preferred therapeutic option, can reduce or avoid the adverse reactions of glucocorticosteroids, and enhance the therapeutic effect of nephrotic syndrome.

Wang Hai et al,[47] in order to observe the effect of modified Qingxin Lianzi Drink on the attenuating and enhancing effect of hormone withdrawal in nephrotic syndrome, selected 70 children with simple nephrotic syndrome during hormone withdrawal in the study and randomly divided them into two groups. One group received treatment with Qingxin Lianzi Drink, while the other group received treatment with Huaiqihuang granules. This study observed that patients receiving Qingxin Lianzi Drink treatment showed significantly reduced urinary protein and improved renal function during the treatment period. It had an adjuvant effect with reduced toxicity, lowered recurrence rate, and improved prognosis.

Wu Mingyue[48] conducted clinical trials and analyzed the clinical efficacy and safety of supplemented Qingxin Lianzi Drink in the treatment of children with nephrotic syndrome during the hormone withdrawal period (Qi-Yin deficiency syndrome), and selected 40 children who met the inclusion and exclusion criteria for study.. While both groups received steroid therapy, the control group was given Huaiqihuang granules orally, while the experimental group received intervention with Qingxin Lianzi Drink. The results showed that modified Qingxin Lianzi Drink could alleviate clinical symptoms in children and was superior to Huaiqihuang granules in reducing the incidence of nephrotic syndrome infection and growth inhibition.

However, it is important to note that these research findings are still preliminary and based on small-scale studies. Therefore, more large-scale, randomized controlled trials are needed to validate the effectiveness of Qingxin Lianzi Drink in treating nephrotic syndrome.

SUMMARY AND SHORTCOMINGS

In pediatric nephrotic syndrome, the use of Western medicine, especially the application of hormones and immunosuppressants to intervene in the disease, can have significant results in some children but also has greater side effects. Long-term application of antibiotics can cause dysbiosis and have significant side effects. In contrast, Chinese medicine has significant advantages in disease intervention, emphasizing the physical conditioning of the patient, focusing on the balance of the environment in the patient's body, and with fewer side effects. The ancient classical formula Qingxin Lianzi Drink can effectively reduce proteinuria and haematuria, regulate immune function, improve resistance, increase the cure rate, reduce the recurrence rate, improve the healing process and have a good safety profile. It has obvious features and advantages in the treatment of some kidney-related diseases, and with the gradual application of modern technology to the study of Chinese medicine, the efficacy of Qingxin Lianzi Drink for kidney diseases is becoming more and more significant, and we should make more efforts to exploit the features and advantages of Qingxin Lianzi Drink.

Key research questions and solutions of Qingxin Lianzi Drink in the treatment of nephrotic syndrome

However, there is currently limited experimental research on the Qingxin Lianzi Drink, and there is an urgent need to strengthen basic research in this area. At the same

time, there are still many unresolved clinical and basic questions regarding nephrotic syndrome, which can be summarized as follows:

(1) Clinical aspects: (a) What are the high-risk populations for nephrotic syndrome? What are the risk factors for developing the disease? (b) What is the efficacy and safety of the Qingxin Lianzi drink in its clinical treatment? (c) What factors contribute to the treatment differences among patients with the same clinical presentation of nephrotic syndrome? (d) Are there still new circulating pathogenic factors?

(2) Basic experimental aspects: (a) What are the mechanisms that influence the progression of nephrotic syndrome? (b) What are the mechanisms by which the main compounds in the Qingxin Lianzi drink affect nephrotic syndrome? Therefore, in future work, conducting clinical trials is an important approach to further explore the necessity of the Qingxin Lianzi drink. Clearly define research objectives, inclusion and exclusion criteria, design randomized controlled trials, recruit sufficient patients, and select appropriate endpoints to evaluate the efficacy and safety of the Qingxin Lianzi drink.

Challenges and solutions of integrated Chinese and Western medicine in the treatment of nephrotic syndrome in children

By fully understanding the pathogenesis of pediatric nephrotic syndrome and combining the dialectic of Chinese medicine with that of Western medicine in clinical treatment, the efficacy and quality of life of children with nephrotic syndrome can be better improved. Meanwhile, Qingxin Lianzi Drink can not only alleviate the side-effects of chemicals and the rebound phenomenon after the withdrawal of chemicals in the treatment of pediatric nephrotic syndrome with chemicals but also strengthen the resistance of the organism to prevent and control the infection and reduce the recurrence of the disease. However, there are some similar challenges in combining Chinese and Western medicine in the treatment of pediatric nephrotic syndrome: (a) Lack of standardized treatment protocols: At present, standardized treatment protocols for combining Chinese and Western medicine in the treatment of pediatric nephrotic syndrome are still limited. Different doctors and institutions may adopt different treatment methods, resulting in inconsistent treatment effects. (b) Limited clinical evidence: although some small-scale clinical studies support the effectiveness of integrated Chinese and Western medicine in treating pediatric nephrotic syndrome, high-quality, large-scale, randomized controlled trials are still lacking. Therefore, more research is needed to evaluate the long-term effects and safety of integrated treatment. (c) Individual differences in treatment: each child may have differences in constitution, condition, and response to treatment. Therefore, individualized treatment strategies need to be considered when formulating treatment plans and adjusted according to the specific conditions of the children. This will greatly benefit further improving the level of integrated Chinese and Western medicine in treating the pediatric nephrotic syndrome.

DATA AVAILABILITY

The experimental data used to support the findings of this study are available from the corresponding author upon request.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest regarding this work.

ACKNOWLEDGMENTS

Any funding did not fund the work.

REFERENCES

1. Veltkamp F, Rensma LR, Bouts AHM; LEARNS consortium. Incidence and Relapse of Idiopathic Nephrotic Syndrome: meta-analysis. [J]. *Pediatrics*. 2021;148(1):e2020029249. doi:10.1542/peds.2020-029249
2. Chen J, Qiao XH, Mao JH. Immunopathogenesis of idiopathic nephrotic syndrome in children: two sides of the coin. [J]. *World J Pediatr*. 2021;17(2):115-122. doi:10.1007/s12519-020-00400-1
3. Esezobor CI, Solarin AU, Gbadegesin R. Changing epidemiology of nephrotic syndrome in Nigerian children: A cross-sectional study. [J]. *PLoS One*. 2020;15(9):e0239300. doi:10.1371/journal.pone.0239300
4. Hong Z. Effects of an intensive drug regimen on laboratory indicators and safety in children with nephrotic syndrome [J]. *Pharm Biotechnol*. 2021;(3):272-274, 290.
5. Sinha A, Bagga A, Banerjee S, et al; Expert Group of Indian Society of Pediatric Nephrology. Steroid Sensitive Nephrotic Syndrome: revised Guidelines. [J]. *Indian Pediatr*. 2021;58(5):461-481. doi:10.1007/s13312-021-2217-3
6. Hölttä T, Jalanko H. Congenital nephrotic syndrome: is early aggressive treatment needed? Yes. [J]. *Pediatr Nephrol*. 2020;35(10):1985-1990. doi:10.1007/s00467-020-04578-4
7. Gao YANG, Shuju LI. Clinical application of Jiawei Qingxin Lianzi Drink in renal system diseases [J]. *Xinjiang Traditional Chinese Medicine*. 2023;41(2):65-66.
8. Zhu LY, Liang YS, Wang SQ. Analysis of Professor Wang Xiaoqin's experience in treating IGA nephropathy with Qingxin Lianzi Drink [J]. *Chin Med*. 2022;11(2):5.
9. Gao W, Zhao H, Zhou Y, et al. Overview of the historical development and modern clinical application of the classical formula Qingxin Lianzi Drink [J]. *Chinese Journal of Experimental Formulas*. 2021;27(9):224-232.
10. Chen B, Hong J. Study on the application of Qingxin Lianzi Drink in kidney-related diseases [J]. *World Digest of Recent Medical Information*. 2020;2(71):187-188.
11. Deng B. *Study on the protective effect of lotus seed heart extract on kidney of diabetic rats and its mechanism*. [D] Chengdu Medical College; 2015.
12. Lei Q, Huang Y, Qian Z, et al. Anti-inflammatory mechanism of scutellaria baicalensis based on network pharmacology [J]. *Chin Herb Med*. 2018;49(15):8.
13. Tunçay SC, Hakverdi G, Şenol Ö, Mir S. Regulatory T-cell Changes in Patients with Steroid-Resistant Nephrotic Syndrome after Rituximab Therapy. [J]. *Saudi J Kidney Dis Transpl*. 2021;32(4):1028-1033. doi:10.4103/1319-2442.338276
14. Liu J, Guan F. B cell phenotype, activity, and function in idiopathic nephrotic syndrome [J]. *Pediatr Res*. 2022;•••:1-9.
15. Trautmann A, Vivarelli M, Samuel S, et al; International Pediatric Nephrology Association. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome. [J]. *Pediatr Nephrol*. 2020;35(8):1529-1561. doi:10.1007/s00467-020-04519-1
16. Kopp JB, Anders HJ, Susztak K, et al. Podocytopathies. [J]. *Nat Rev Dis Primers*. 2020;6(1):68. doi:10.1038/s41572-020-0196-7
17. Campbell RE, Thurman JM. The Immune System and Idiopathic Nephrotic Syndrome. [J]. *Clin J Am Soc Nephrol*. 2022;17(12):1823-1834. doi:10.2215/CJN.07180622
18. Ahmadian E, Rahbar Saadat Y, Dalir Abdolahinia E, et al. The Role of Cytokines in Nephrotic Syndrome. [J]. *Mediators Inflamm*. 2022;2022:6499668. doi:10.1155/2022/6499668
19. Ye Q, Wang DJ, Lan B, et al. T-cell and B-cell repertoire diversity are selectively skewed in children with idiopathic nephrotic syndrome revealed by high-throughput sequencing [J]. *World J Pediatr*. 2022;•••:1-10.
20. Gauckler P, Shin JI, Alberici F, et al; RITERM study group. Rituximab in Membranous Nephropathy. [J]. *Kidney Int Rep*. 2021;6(4):881-893. doi:10.1016/j.ekir.2020.12.035
21. Basu B, Angeletti A, Islam B, Ghiggeri GM. New and Old Anti-CD20 Monoclonal Antibodies for Nephrotic Syndrome. Where We Are? [J]. *Front Immunol*. 2022;13:805697. doi:10.3389/fimmu.2022.805697
22. Zhu B, Zhang R, Yang H, et al. Association of HLA-DQA1 gene polymorphisms with the risk of children primary nephrotic syndrome in Chinese population. [J]. *J Clin Lab Anal*. 2019;33(1):e22623. doi:10.1002/jcla.22623
23. Hejazian SM, Zununi Vahed S, Moghaddas Sani H, et al. Steroid-resistant nephrotic syndrome: pharmacogenetics and epigenetic points and views. [J]. *Expert Rev Clin Pharmacol*. 2020;13(2):147-156. doi:10.1080/17512433.2020.1702877
24. Dufek S, Cheshire C, Levine AP, et al. Genetic Identification of Two Novel Loci Associated with Steroid-Sensitive Nephrotic Syndrome. [J]. *J Am Soc Nephrol*. 2019;30(8):1375-1384. doi:10.1681/ASN.2018101054
25. Trautmann A, Vivarelli M, Samuel S, et al; International Pediatric Nephrology Association. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-resistant nephrotic syndrome. [J]. *Pediatr Nephrol*. 2020;35(8):1529-1561. doi:10.1007/s00467-020-04519-1
26. Tamura H. Trends in pediatric nephrotic syndrome. [J]. *World J Nephrol*. 2021;10(5):88-100. doi:10.5527/wjn.v10.i5.88
27. Wang CS, Greenbaum LA. Nephrotic Syndrome. *Pediatr Clin North Am*. 2019;66(1):73-85. doi:10.1016/j.pcl.2018.08.006
28. Chen F, Tao W. Thunder fire moxibustion combined with warming the spleen and kidney method for the treatment of spleen and kidney yang deficiency in primary nephrotic syndrome [J]. *Journal of External Treatment of Traditional Chinese Medicine*. 2021;30(2):2.
29. Wang YG. Clinical value of spleen tonifying and kidney benefiting soup combined with warm acupuncture in treating diabetic nephrotic syndrome with spleen and kidney yang deficiency [J]. *Chinese Convalescent Medicine*. 2021;30(8):828-830.
30. Zhijie GUO, Bin NI. Effects of blood-boosting and water-eliminating soup combined with western medicine on Chinese medicine indexes and renal function indexes in patients with primary nephrotic syndrome [J]. *Chinese Medicine Clinical Research*. 2021;13(5):3.

31. Rui G, Jun G, Ling S, et al. Efficacy and effect on serum immunoglobulin and complement in the treatment of nephrotic syndrome by adding and subtracting ginsengqi dihuang tang [J]. *Shaanxi Traditional Chinese Medicine*. 2022;43(8):4.
32. Chen Q. Analysis on the clinical effect of clearing heat, resolving stasis and tonifying kidney soup in treating patients with proteinuria in nephrotic syndrome [J]. *Heilongjiang Science*. 2021;12(2):54-55.
33. GUAN Yulong, Deng Fan, WANG Xiaoqin. Proceedings of Professor Wang Xiaoqin's addition and subtraction of Qingxin Lianzi Drink. [J]. *Asia-Pacific Traditional Medicine*. 2023;19(2):4.
34. Wenchao LI, Xue LI. Clinical observation on early diabetic nephropathy treated by adding and subtracting Qingxin Lianzi Drink[J]. Heilongjiang traditional. *Chin Med*. 2021;50(1):2.
35. Jian WANG, Zhenzhen ZHANG, Xiuzhen MEI, et al. Progress of antibacterial effects and mechanisms of flavonoids [J]. *Jiangsu Nongye Kexue*. 2023;51(1):1-8.
36. Fang Yi-Wei. Discussion on the treatment of chronic kidney disease with Qingxin-Lianzi Drink based on the elevation of qi[J]. Chinese Science and Technology Journal Database (Full Text Edition) Medicine and Health,2022(12):0261-0264.
37. Yue XIA, Xiaorong NI, Xia PENG, et al. Discussion on the application of lotus seed heart in gynaecological diseases based on the "heart-kidney-uterus axis" [J]. *Hebei Traditional Chinese Medicine*. 2021;43(12):2081-2084.
38. Wang H, Jiang Q, Zhang L. Baicalin protects against renal interstitial fibrosis in mice by inhibiting the TGF-β/Smad signalling pathway. *Pharm Biol*. 2022;60(1):1407-1416. doi:10.1080/13880209.2022.2097700
39. Ning X, Luo D, Chen Y, Shao Y, Xu J. Baicalin Reduces Renal Inflammation in Mesangial Proliferative Glomerulonephritis through Activation of Nrf2/ARE and PI3K/AKT Pathways. *Discov Med*. 2023;35(176):372-382. doi:10.24976/Discov.Med.202335176.38
40. Hou-Sheng ZHENG, Ying-Ping WANG, Si-Wen ZHENG, et al. Exploring the immunomodulatory mechanism of ginseng based on network pharmacology [J]. *China Hospital Drug Evaluation and Analysis*. 2019;19(12):1435-1440.
41. Guo J, Wang R, Min F. Ginsenoside Rg1 ameliorates sepsis-induced acute kidney injury by inhibiting ferroptosis in renal tubular epithelial cells. *J Leukoc Biol*. 2022;112(5):1065-1077. doi:10.1002/JLB.1A0422-211R
42. Zhou Q, He X, Zhao X, et al. Ginsenoside Rg1 Ameliorates Acute Renal Ischemia/Reperfusion Injury via Upregulating AMPKα1 Expression. *Oxid Med Cell Longev*. 2022;2022:3737137. doi:10.1155/2022/3737137
43. Sung-gun JANG, Hak-mu JANG, Young-sil PARK. Current status of research on the pharmacological effects of ginsenosides on precancerous lesions [J]. *Chin J Clin Pharmacol*. 2022;38(11):1283-1286.
44. Haifeng WEI, Yanhong WEI, Yunqian LI, et al. Inhibitory effect of tannic acid on the expression of inflammatory factors in renal tissues of diabetic rats [J]. *Jilin Daxue Xuebao Yixue Ban*. 2011;37(3):5.
45. Yuan YUAN, Yu GAN, He HUANG, et al. Antihypertensive effect of aqueous extract of Chinese medicine dijiangpi on spontaneously hypertensive rats and its mechanism [J]. *Chinese Journal of Traditional Chinese Medicine*. 2018;36(11):3.
46. Yongzheng ZHANG, Hai WANG, Yanyan CHEN, et al. Experimental study on the treatment of adriamycin nephrotic syndrome in rats by adding flavour Qingxin Lianzi drink [J]. *World Traditional Chinese Medicine*. 2021;16(16):2408-2412.
47. Wang H, Wu MY, Zhang YZ. Clinical study on the treatment of nephrotic syndrome during hormone withdrawal by adding flavour Qingxin and lotus seed drink[J]. *Chinese paediatrics with integrated Chinese and Western medicine*, 2021, 13(1):76-79.
48. Wu M. *Clinical study on the treatment of children with nephrotic syndrome during the hormone withdrawal period by adding flavour Qingxin and lotus seed drink*. [D] Heilongjiang University of Traditional Chinese Medicine; 2021.