

# Research Progress of Traditional Chinese Medicine in the Treatment of IgA Nephropathy

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**Abstract:** *The treatment of IgA nephropathy (IgAN) is difficult, and modern medicine is still not clear about its etiology and pathogenesis. Traditional Chinese medicine(TCM) plays an important role in the treatment of IgAN, the use of "poison damage of renal collaterals", from the wind treatment, general use, "mediation trijiao", treating IgAN from the pharynx, spleen and kidney, intelligent door as well as five zang-organs make , the selection of Zhuling decoction, Banxia-xixin decoction, Shenqi-Dihuang Decoction, Guben-Tongluo Decoction and other classic and experience prescriptions, trijiao acupuncture, invigorating spleen and kidney acupuncture treatment, etc. TCM such as diet therapy can control clinical symptoms such as hematuria, proteinuria and hypertension caused by IgAN, and further control and delay the progress of IgAN.*

**Keywords:** IgA nephropathy, Chronic glomerulonephritis, Traditional Chinese medicine, Treatment based on pattern differentiation.

## 1. Introduction

The main purpose of clinical treatment of IgA nephropathy (IgAN) is to control the main symptoms of IgAN, such as hematuria, proteinuria and hypertension, delay and control the progression of IgAN [1]. Traditional Chinese medicine (TCM) plays a positive role in controlling and delaying the development of IgAN and has good clinical efficacy.

## 2. Understanding of Etiology and Pathogenesis of IgAN in TCM

IgAN is named after the characteristic immunopathology, and its pathological phenotype is more, the main clinical symptoms are hematuria, proteinuria, edema, hypertension, impaired kidney function, etc. It is a group of clinicopathologic syndromes composed of clinical and pathological. Its clinical symptoms were also recorded in the medical literature of the motherland in the past dynasties, such as "blood in urine", "turbidness in urine", "kidney wind", "vacuity strain" and "low back pain" [2].

Hematuria was described as "drowning blood" and "urine blood" in the literature of past dynasties. The name of "urine blood" was put forward in the Jin-Gui yao lue (Synopsis of the Golden Chamber). Exogenous wind and heat, dampness and heat, long illness consuming vital qi can lead to hematuria [3].

Proteinuria in past dynasties literature there is no record, TCM believes that its main is renal dysfunction of sealed solid is taken as a result of "nutrients or drainage", the occurrence of proteinuria and abnormal lung spleen and kidney, the sanjiao (triple energizer) gasification disorder. The physiological structure and function of the kidney are in great agreement with the theory of collateral disease. The theory of collateral disease holds that "collateral depression" is the main cause of proteinuria [4].

Edema refers to the retention of fluid caused by the disorder of fluid metabolism in the body. Both exogenous factors such as wind and water dampness and internal injury factors such as

emotion and diet can lead to edema. It is mainly related to lung, spleen, kidney and three organs [5]. Clinically, according to the different sites of edema and different syndrome types, the treatment principles and methods are also different. Dialectical treatment of IgAN patients should also pay attention to the treatment of edema.

Hypertension can accelerate the damage of heart, brain and kidney, and is also the main symptom of IgAN. The main pathogenesis of IgAN hypertension is the deficiency of liver and kidney caused by a long illness, the imbalance of Yin and Yang, and the deficiency of Yin and Yang. The main manifestations are headache, vertigo and other symptoms, which need to be treated according to the clinical symptoms and syndrome and treatment classification [6].

The different clinical symptoms of IgAN need both holistic consideration and dialectical treatment. TCM can play this advantage in the treatment of IgAN, and make full use of the holistic thinking of TCM and the concept of syndrome differentiation and treatment to analyze its etiology and pathogenesis can better guide clinical treatment.

## 3. IgAN's Dialectical Treatment of Chinese Medicine

Dialectical treatment plays an important role in the process of Chinese medicine treatment of IgAN, accurate evidence type of dialectical treatment for patients tend to have a good clinical curative effect. At present, the rigor and scientificity of TCM clinical syndrome differentiation and treatment guidelines for IgAN have been greatly improved, but the syndrome standardization and evidence evaluation system are still in the process of research and improvement [7]. IgAN itself also has certain regional differences, and its treatment methods are also different. Many doctors have formed their own unique dialectical thinking and experience in their own diagnosis and treatment process and clinical research.

### 3.1 Dialectical Thinking and Academic Views

Ren Jixue [8] the viewpoint of "poison damage of renal

collaterals" is the treatment of IgAN, it considers the six evils of the exogenous pathogenic and internal injuries of sputum poison, toxic heat long illness, etc all can lead to "poison damage of renal collaterals". IgAN can be treated from the "kidney wind", which can be divided into acute stage, remission stage, and chronic protracted stage. According to the different development of the disease in each period and the patient's physical condition, it can be treated dialectically to achieve the purpose of expelling toxic pathogens and toning healthy qi. Liu Hongfang [9] has similarities in the treatment of IgAN from the perspective of latent pathogens and "toxic damage to the kidney collaterals". The staging of IgAN is the same, and the causes of IgAN are also divided into six exogenous pathogens leading to latent pathogens and the internal movement of latent pathogens caused by the deficiency of positive qi. According to different stages, the three treatments of "cleansing, penetrating and nourishing-supporting" are adopted.

Zhang yu [10] think IgAN proteinuria should be treated from the wind, the concrete from the wind, endogenous wind disturbance, FuFeng secondary to these three aspects to syndrome differentiation and treatment, the good and the number change, so the patients also is repeated, deferment refractory, expelling wind outside the drug should be used clinically, such as herba schizonepetae, windproof, and cane drugs; The drugs to calm the internal wind, gastrodia, keel and oyster; Functions of t2dm with drugs, for example, scorpion, centipede, lumbricus; Medicines that benefit qi and strengthen the surface, such as Codonopsis ginseng, Astragalus membranaceus, Atractylodes rhizoma, and windproof; In clinical practice, the use of wind medicine should also pay attention to its dryness and irritability, which consumes Yin and body fluid, and should be used to nourish Yin and nourish blood.

Wang Chen [11] put forward the view of "general use" in the process of clinical diagnosis and treatment. He believed that the disorder of Sanjiao gasification caused by the deficiency of the body and the excess of external pathogens is one of the causes of IgAN. After the upper jiaoyu lung defense is infected with pathogens, it is not cured for a long time, and the middle jiaoyu spleen and stomach are affected, the spleen is lost to transport, phlegm turgor and toxic pathogens accumulate in the body, which also damages the body's vital qi and causes the occurrence of the disease. This is the cause of Sanjiao obstruction. According to the different locations, the treatment of upper focus on the lung, middle focus on the spleen, and lower focus on the kidney is proposed. After a long illness, it is easy to enter the collaterals. Professor Wang Chen also attaches importance to the theory of collaterals and puts forward the view of "dredging collaterals", and attaches importance to the use of worm drugs and rattan drugs for "dredging collaterals". This view is also consistent with Li Lin et al. [4] 's research on IgAN and renal collaterals stasis, and the formation of "collaterals depression" after a long illness. Wang Chen also believes that the obstruction of six meridians is also related to the progression of IgAN. After the pathogen first attacks the sun, it eventually leads to the pathogen attacking Jueyin through transmission, and the disease is difficult to cure. Therefore, clinical attention should be paid to the early treatment of the disease to prevent the spread of the disease.

Chen Yiping [12] "mediation trijiao" therapy also paid attention to reconciling Shaoyang, regulating sanjiao qi, and used Xiaobupleurum decoction to treat IgAN. Studies have shown that the treatment of IgAN patients should not simply focus on the local treatment of the kidney, but more attention should be paid to improving the abnormal glycosylation of IgA and clearing the IgA1 immune complex in the mesangial region of the kidney [13]. "Mediation trijiao" therapy from the trijiao treatment, through the suppression of respiratory mucosa, gastrointestinal mucosa, urethra mucosa immune abnormalities caused by abnormal IgA glycosylation; The IgA immune complex was cleared by means of reconciliation and profit thinning.

Zou Yanqin [14] put forward the view of treating IgAN from the pharynx, spleen and kidney, pharyngeal and feet shaoyin kidney after close, invaded from the upper attacks throat, throat is also the human ego to protect barrier, modern medicine also think pharyngeal tonsils are important immune organs, tonsil abnormal immune response associated with IgAN also, Tonsillectomy is also one of the means of modern medical clinical treatment of IgAN patients [15]. In the treatment of spleen, the deficiency of spleen temperament is mainly considered, which leads to the decrease of spleen function such as transportation and circulation, and fixation and absorption of qi, and then leads to the increase of proteinuria, hematuria and edema. The reason for treatment based on kidney is that the kidney and bladder are external and internal, and the deficiency of kidney qi leads to bladder dysfunction, urine metabolism disorder, and long-term illness and kidney, congenital damage, clinical should pay special attention to the prevention and treatment of kidney.

Cai-feng zhu [16] using the theory of "intelligent door as well as five zang-organs make" dialectical treatment of patients with IgAN, it considers intelligent door is closely related to the large intestine, has the function of conduction e. dregs the normal operation of intelligent door is closely connected with five viscera qi activity of smooth adjustment. Intelligent door impassability, five viscera qi activity dysfunctional, and eventually the original qi will damage to the kidney, IgAN low five zang-organs function in patients with a long illness, accumulation of phlegm turbidity toxin factor if the body is not able to through the intelligent door, also can cause a great burden for patients with kidney; Modern medicine also believes that the gut, as the largest immune organ of the human body, is closely related to the kidney. Some studies have shown that the imbalance of intestinal flora can cause serious harm to the kidney.

### 3.2 Classical and Empirical Prescriptions

In the treatment of IgA nephropathy patients with damp-heat type, Zhuling decoction combined with Xiaoji Yinzi can effectively reduce proteinuria and hematuria, delay and control the development of patients' disease, prevent secondary edema and hypertension caused by massive proteinuria and hematuria, effectively improve the filtration function of glomeruli and control the fibrosis process of glomeruli and renal tubules [17]. Yang Xiaohong et al. [18], based on the theory of "one qi circulates and four images are generated by soil", believed that attention should be paid to regulating the spleen and stomach of middle jiao to treat

hematuria, and the symptom of IgAN hematuria should be treated by raising soil to dry dampness, raising wood to achieve depression, and draining water and heat. In addition, the combination of Zhuling Decoction and Shenyan-Kangfu tablet can also effectively improve the proteinuria of IgAN patients with qi and Yin deficiency and spleen and kidney deficiency [19].

Banxia-Xixin Decoction has positive significance in treating patients with gastrointestinal disharmony caused by spleen deficiency and stomach weakness and cold and heat disorder of IgAN. Modern medical research believes that IgAN has the function of regulating immune factors and repairing intestinal mucosa, which provides certain scientific basis for the theory that the pathogenesis of IgAN is related to intestinal mucosal immunity [20]. The use of Huangqi Guizhi Wuwu Decoction for IgAN patients with spleen-kidney Yang deficiency can effectively relieve symptoms such as cold limbs and weak lumbar acid [21], and experimental studies have proved that Huangqi Guizhi Wuwu decoction has a protective effect on kidney podocytes [22]. Ephedrine and forsythia Chixiaodou Decoction used in the treatment of IgAN has the effect of resolving evil and clearing heat and dampness. In IgAN patients, kidney qi is damaged, which damages lung and spleen and viscera, and tri-jiao gasification is weak, water is suspended in the body, and heat is transformed in the body. The use of ephedrine and forsythia Chixiaodou decoction has the effect of lifting the pot and removing the lid, and it is conducive to the recovery of tri-jiao gasification function by opening lung qi and clearing the water channel [23].

Shenqi-Dihuang Decoction has been clinically recognized and adopted by many doctors to treat patients with IgAN Qi and Yin deficiency. Shenqi-Dihuang Decoction can reduce proteinuria and hematuria in IgAN patients, and protect kidney and control fibrosis [24-27]. Pharmacological studies have found that Shenqi- Dihuang Decoction can resist virus, tumor and inhibit inflammation [28]. The doctors make dialectical treatment according to the different factors such as the patient's personal constitution and the different stages of the development of the disease, and give the treatment of addition and subtraction. Nie Lifang [29] Nie's Supplemented Shenqi-Dihuang Decoction, an empirical prescription for treating nephropathy, has a good effect of invigorating qi and Yin, invigorating spleen and kidney, and believes that it can significantly improve the symptoms of chronic qi deficiency weakness, listless spirit, waist and knee weakness, night sweats and other symptoms common in IgAN patients with Qi and Yin deficiency. Nie Lifang often uses raw rehmannia instead of cooked rehmannia to treat patients with Yin deficiency and internal heat type to prevent excessive dampness. Raw Rehmannia also has multiple effects such as reducing serum creatinine, urinary protein and glomerular fibrosis degree, and protecting mesangial cells [30].

Guben-tongluo prescription is an empirical prescription from the nephrology Department of Shuguang Hospital of Shanghai University of Traditional Chinese Medicine. Based on the "Xuanfu theory", Guben-tongluo prescription is used to treat IgAN by supplementing Qi and strengthening exterior, promoting blood circulation and Tongluo. It has been proved that Guben-tongluo formula can reduce proteinuria and protect kidney. By increasing podocin and decreasing

$\alpha$ -actinin-4 expression, B7-1 activation is prevented by the immune pathway, and the expression level of serum B7-1 is further reduced, thus maintaining the normal structure and function of podocin [31].

Chansu-Dihuang decoction is based on Liuwei Dihuang pill, which combines cicada and Suye to dispel the wind and dissipate the pathogenic factors, and eliminate the latent wind. Astragalus membranaceus gas-solid table, water swelling; Chuanxiong Huoxue qi, the combination of all drugs, addition and subtraction of cut. Experimental studies have shown that Chansu-Dihuang decoction can inhibit autophagy of renal podocytes and delay the progression of chronic kidney disease [32].

### 3.3 Acupuncture Treatment

In the study of renal fibrosis caused by hypertensive renal damage, Yang Shaozheng used the method of Fuzheng-huoxue, and acupuncture Shenshu (BL 23) and Geshu (BL 23) was used to strengthen spleen and kidney, activate blood circulation and channel collaterals [33]. This study showed that acupuncture Shenshu and Geshu could also inhibit the expression of promoting factors of renal fibrosis, which had a positive significance in guiding the treatment of IgAN.

Han Yingying et al. conducted a clinical study on patients with insomnia caused by chronic kidney disease [34]. Trijiao acupuncture was applied to treat the patients at Danzhong (CV 17), Zhongwan (CV 12), Qihai (CV 6), Xuehai (CV 10), Zusanli (ST 36) and Waiguan (CV 6). All the acupoints are combined to achieve the effect of nourishing qi and regulating blood, consolidating Ben and strengthening yuan. So that Yin and Yang harmony, Yang into Yin sleep.

Acupuncture and moxibustion therapy combined with prescription has a good effect on improving the symptoms of IgAN patients. Ni Jiaqing clinical study combined the invigorating spleen and kidney acupuncture with the Shi PI Gushen Huayu decoction, and used Guanyuan (CV 4), Mingmen (GV 4), Sanyinjiao (SP 6), Zusanli (ST 36), Shenshu (BL 23) and Pishu (BL 23) in the treatment of proteinuria, which has a good effect on invigorating the spleen and tonifying the kidney [35].

### 3.4 Diet Treatment

The dietary intake of IgAN patients is significantly related to the control of the disease. In clinical practice, we should not only pay attention to the drug treatment of patients, but also pay more attention to the diet control and education of IgAN patients.

Professor Huang Chunlin has a unique view on the diet control of IgAN patients. In addition to the common diet control principles of kidney disease patients, such as the principle of high-quality low protein intake, low salt, low gluten, low purine, low fat and high vitamins, Professor Huang Chunlin also uses the principle of dialectical diet therapy of TCM to guide the dietary intake of patients [36].

For example, patients with gross hematuria take clearing heat,

cooling blood and hemostasis as the treatment method, and have the symptoms of wind and heat in the upper-jiao, they can use pear, radish, bitter melon, etc. Dampness and heat in the middle-jiao, can use coix seed, dolichos lablab, red beans, Rhizoma Dioscoreae, Gorgon euryale seed to achieve the role of clearing heat, eliminating dampness and tonifying spleen; Damp heat in the lower-jiao, can be given Oldenlandia diffusa, cogongrass rhizome, fresh lotus root, zucchini and other heat-cleaning and dampness-eliminating products. Studies have shown that IgAN patients with Deficiency of kidney-yin and dampness-heat syndrome, for example, should eat raw soybeans made into tofu and soybean milk, and avoid the use of cooked soybeans and their products. Also can take deep sea fish and shellfish, has the function of nourishing Yin, soft firm loose knot. Some fungi can also be eaten to achieve the effect of nourishing qi and Yin, supplementing spleen and qi. For example, hericium mushroom has the effect of nourishing temper and nourishing kidney essence.

#### 4. Experience in IgAN's use of Chinese Medicine and Chinese Medicine Preparations

Based on the TCM inheritance arithmetic platform, LAN Yak analyzed the medication rules of Song Liqun for IgAN, and found that its medication was mainly based on the nature of Gan and ping, and the meridians were mainly the three meridians of liver, spleen and kidney, and its effects were mainly tonifying deficiency, astringent and digestion [37]. The analysis showed that the main treatment direction was Ganping tonifying, strengthening spleen, tonifying liver and kidney. In addition, Professor Song Liqun believed that it is necessary to timely choose burdock seed, golden buckwheat and other clear throat to prevent the spread of disease, and also address both the symptoms and root causes of the problem, and use Rosa laevigata, Gorgon euryale seed and other astringent drugs while using kidney tonic drugs.

ZhengQingFengTongNingPian combined with hydroxychloroquine in the treatment of IgAN can effectively improve the renal function index and reduce the serum IgA level. ZhengQingFengTongNingPian is extracted from caulis sinomenii. Modern pharmacological studies have shown that sinomenine has immunosuppressive effect, which can reduce the glomerular immune response and protect the glomeruli. It also has anticoagulant effect, which helps to regulate renal blood flow and reduce renal function damage. Its combination with hydroxychloroquine can enhance immunosuppression, reduce IgA level and control proteinuria [38].

Astragalus injection and Astragalus granules combined with western medicine can improve the clinical effect and laboratory indexes in the treatment of IgAN [39]. Network pharmacology was used to screen the targets and signaling pathways of Astragalus and Cordyceps sinensis in the treatment of IgAN, and experiments verified that astragalus and Cordyceps sinensis in the treatment of IgAN may act on VEGFA, HIF1A and other key targets, and inhibit renal fibrosis and delay the development of IgAN through multiple molecular targets and multiple pathways [40].

In the treatment of IgAN patients, Shenqi-Fuzheng injection and Ligustrazine injection have significant effects on reducing

Scr level, BUN level and urine protein level, and the effect of combined use of TCM injection and conventional western medicine treatment is greater than either used alone [41].

Huangkui capsule, Tripterygium glycoside tablets, Jinshuibao capsule and other Chinese patent medicine by Lou Yan network meta-analysis, its combined use with ACEI and ARB drugs is significantly better than the simple conventional treatment of western medicine, the combined treatment of anti-inflammatory, anti-oxidation, protection of renal function has a positive effect. Wang Ruiqi et al. demonstrated that Shenfukang II capsule could inhibit the proliferation of endothelial cells in renal arterioles and alleviate kidney injury [43].

#### 5. Summary

TCM treatment of IgAN has its irreplaceable advantages. Many doctors have mature theoretical guidance and clinical experience in dialectical treatment and treatment of IgAN. TCM theoretical knowledge plays an indispensable role in guiding its dialectical treatment and prescription research. Further research on the treatment of IgAN by TCM should be carried out in the future. However, some methods and means of TCM treatment of IgAN still lack certain clinical guidelines, and evidence-based medical research and clinical trial research should be strengthened. Some studies on the treatment of IgAN with TCM prescriptions and proprietary Chinese medicine also have problems such as small sample size and insufficient evidence evaluation. In the future, larger sample size, more standardized experimental design and clinical research methods can be used for research.

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