

Progress in Traditional Chinese and Western Medicine of IgA Nephropathy

Juan Wang^{1,a}, Xiaoyong Yu^{2,b,*}

¹Shaanxi University of Chinese Medicine, Xi'an, Shaanxi, 712046, China

²Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an, Shaanxi, 710003, China
^a741734706@qq.com, ^bgub70725@126.com

*Corresponding author

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Abstract: IgA nephropathy is a renal disease characterized by glomerular IgA deposition, with proteinuria, hematuria, hypertension or renal impairment as the main clinical manifestations, and its incidence increases with age. At present, the cause of IgA nephropathy is not completely understood and there is no specific treatment. The pathogenesis and clinical treatment of Traditional Chinese medicine and western medicine have their own theories and advantages. Now the etiology and pathogenesis of IgA nephropathy and the treatment of Traditional Chinese medicine are reviewed, in order to provide theoretical basis and reference for the clinical treatment and research of IgA nephropathy.

1. Introduction

IgA nephropathy is a renal disease mainly characterized by glomerular IgA deposition. It is one of the most common primary glomerular diseases worldwide, and its incidence increases with age. As shown in Figure 1, IgA nephropathy usually shows proteinuria, hematuria and hypertension, sometimes with renal impairment. At present, the cause of IgA nephropathy is not completely clear, and there is no specific treatment method. The treatment is mainly for the symptoms and causes, to reduce the symptoms and delay the progression of the disease. Traditional medicine attributes IgA nephropathy to "kidney wind", "low back pain", "urine blood", "edema" and other categories, and its overall thinking and dialectical treatment, so as to regulate the internal environment of the human body, enhance kidney function and improve blood circulation. Western medicine believes that it may be related to genetic, infection, environmental, abnormal immune function, and other factors. Commonused treatment methods include controlling hypertension, reducing proteinuria, use of immunosuppressive agents, etc., to effectively control the disease and slow down the progress of the disease. Both Chinese and western medicine can combine the specific situation of patients for individualized treatment, in order to achieve the best treatment effect.

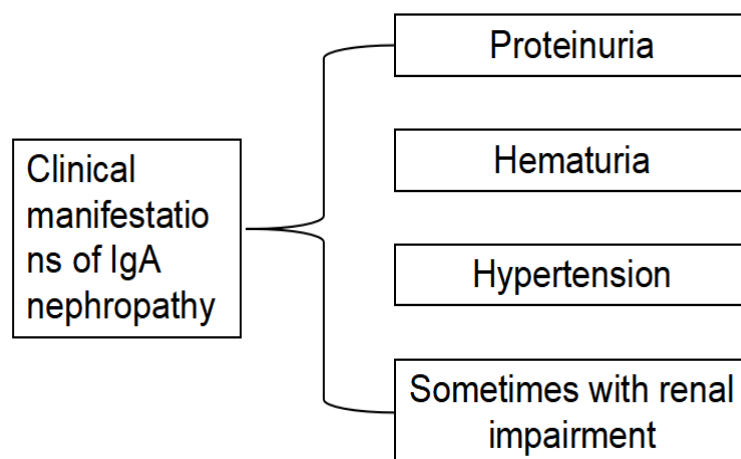


Figure 1: Clinical manifestations of IgA nephropathy

2. Knowledge of nephropathy in IgA in traditional Chinese medicine

2.1. Etiology and mechanism of IgA nephropathy

IgA nephropathy is a disease with hematuria accompanied by different degrees of proteinuria and renal impairment. The traditional medicine does not have the name of IgA nephropathy. According to the clinical characteristics, it is attributed to the categories of "kidney wind", "low back pain", "urine blood", "edema" and other categories. This disease is the evidence of this deficiency standard, this deficiency is kidney deficiency and spleen deficiency, the standard solid is dampness and heat with blood stasis, phlegm turbidity. The Synopsis of the Golden Chamber records: "The kidney is the main water, and the spleen is the main soil. Water flooding is soil waterlogging, soil waterlogging is water flooding. Kidney qi deficiency can not make water, temper deficiency can not transport soil, so the water and soil waterlogging. Its disease is edema", spleen and kidney Yang deficiency leads to deficiency of qi and blood, kidney qi is not solid, thus affecting the normal function of the kidney, leading to the occurrence of IgA nephropathy. Hot heat and phlegm turbidity are important factors in the onset of IgA nephropathy; factors such as exogenous addiction, poor diet, humid living environment, emotional instability cause damp heat accumulation in the body, causing pathological changes such as qi stagnation, blood stasis, phlegm and turbidity, thus affecting the normal function of the kidney and leading to IgA nephropathy. Different experts have different views on the etiology of the disease. Both Professor Zhang Qi and Professor Nie Lifang emphasized the TCM etiology and mechanism of IgA nephropathy, including Professor Zhang Qi [1] believes that the etiology and pathogenesis are related to heat, which are inseparable from deficiency and blood stasis. In the attack period, wind and heat cause the lung or hot, or dampness and heat stasis lead to collateral injury and blood overflow; in the chronic persistent stage, the deficiency of spleen and kidney is the main pathogenesis. Nie Lifang [2] believes that the causes of IgA nephropathy is mostly in the spleen and kidney deficiency, congenital deficiency, dietary disorders, seven emotions and other factors to consume the healthy qi, resulting in the immune function of the body. Its inducement is mostly external evil and overwork, protracted lesions, and eventually lead to repeated attacks of hematuria.

In general, traditional Chinese medicine scholars believe that the etiology and pathogenesis of IgA nephropathy are multifaceted, as shown in Figure 2, which includes congenital deficiency, poor diet, poor mood, environmental factors and other aspects. In terms of treatment, differentiation and treatment should be made from the aspects of deficiency and excess. Individualized treatment

should be carried out according to the specific situation of the patient, regulating qi, blood, yin and yang to achieve the goal of preventing and treating the disease.

2.2. TCM treatment of IgA nephropathy

With the development of traditional Chinese medicine, traditional Chinese medicine has the advantages of diverse components, small adverse reactions and wide action targets. Studies have proved that traditional Chinese medicine, compound and TCM characteristic therapy have achieved remarkable results on the treatment of IgA nephropathy.

The main function of acupuncture and moxibustion in the treatment of IgA nephropathy is to adjust the balance of qi, blood, Yin and Yang, promote the self-repair function of the body and improve immunity, so as to achieve the purpose of treating and preventing IgA nephropathy. The literature [3] have shown that in the treatment of IgA nephropathy, the commonly used acupoints are Zusanli, Shangwan, Shangwan, Zhongwan, Qihai, Shenque, Guan Yuan, Renyu, etc. Numerous studies [3-4] have shown that in the treatment of IgA nephropathy, commonly used drugs include the following five categories: heat clearing and detoxification: honeysuckle, forsythia, wild chrysanthemum, Coptis, baicalensis, gardenia, etc. Promoting blood circulation and removing blood stasis: peach kernel, safflower, Chuanxiong, Salvia miltiorrhiza, Panax notoginseng, etc. Supplements: ginseng, astragalus, Astragalus, dangshen, ripe ground, angelica, atractylodes, etc. Li water through lymph: diarrhea, car, front son, wood, poria cocos, etc. Harmony viscera: yam, barbary wolfberry, andra chinensis, longan meat, mulberry and so on .The TCM classification for treating IgA nephropathy is shown in Table 1. Among them, astragalus, pseudostellariae, Chinese yam, poria, atractylodes, Eucommia ulmoides, lotus chinensis, rhizana, ripe rehmannia and so on are often used in the treatment of IgA nephropathy, and have significant curative effect [5]. Under the principle of holistic thinking and dialectical treatment, different experts and professors have put forward their own dialectical treatment theory and clinical application in the treatment of IgA nephropathy in traditional Chinese medicine. For example, Chen Yiping [6] divided IgA nephropathy into the acute and chronic phases. In the acute period, the wind and heat are mainly disturbed, in the treatment of wind and heat, and in the chronic period, qi deficiency and Yin deficiency are mainly used, and in the treatment, four gentleman soup and peach red four things soup are used to replenish qi and promote blood circulation. Wang Yaoxian [7] suggested the treatment of three kinds of coke IgA nephropathy, early treatment of heart and lung, late treatment of liver and kidney. Du Jinxing [8] divided the treatment of IgA nephropathy into three stages, the initial focus of the wind heat, with silver warping powder or jing resistance scattered; hot outside the cold, should choose ephedra red bean soup, small dragon soup and gypsum; long living in wetland or cold damp rheumatism, to add Elsholtzia drink. For those with moderate heat and dampness in the middle stage, add or subtract Baitouweng Tang or Gegen Qinlian Tang. In the later stage of the disease, when the disease lasts for a long time, Proteinuria is the main form, while in the case of low proteinuria and mild edema, Wuling San Wan and Shenling Baizhu Powder are often used. For those with high urinary protein content and severe edema, Zhenwu Tang with warm yang and diuretic effects should be used. Those with obvious Hypoproteinemia should use Danggui Buxue Decoction. If the disease is mainly hematuria for a long time, Liu Wei Di Huang Wan and Zhibai Dihuang Pill should be added or subtracted.

In general, according to the onset of the disease, the disease is generally divided into acute phase and chronic phase or divided into early, middle, late three stages, so in the treatment is generally the first stage syndrome differentiation treatment, and then syndrome differentiation treatment. The dialectical treatment of different experts in IgA nephropathy are shown in Figure 2. At the same time, attention should be paid to the dosage and compatibility of drugs to avoid improper use of

traditional Chinese medicine or adverse reactions. In the course of treatment, a reasonable diet and lifestyle changes should also be combined to achieve the best treatment effect.

Table 1: Traditional Chinese medicine classification for the treatment of IgA nephropathy

Classification of TCD	Commonly used traditional Chinese medicine
Clearing away heat and toxic material	Honeysuckle, forsythia, wild chrysanthemum, coptis, Scutellaria baicalensis, gardenia, etc.
Promoting blood circulation and removing blood stasis	Peach kernel, safflower, xiong chuanxiong, Salvia miltiorrhiza, Panax notoginseng, etc.
Tonifying	Ginseng, astragalus, dangshen, ripening ground, angelica, atractylodes, poria cocos, etc.
Reconciliation of viscera	Yam, barbary wolfberry, schisandra chinensis, longan meat, mulberry, etc

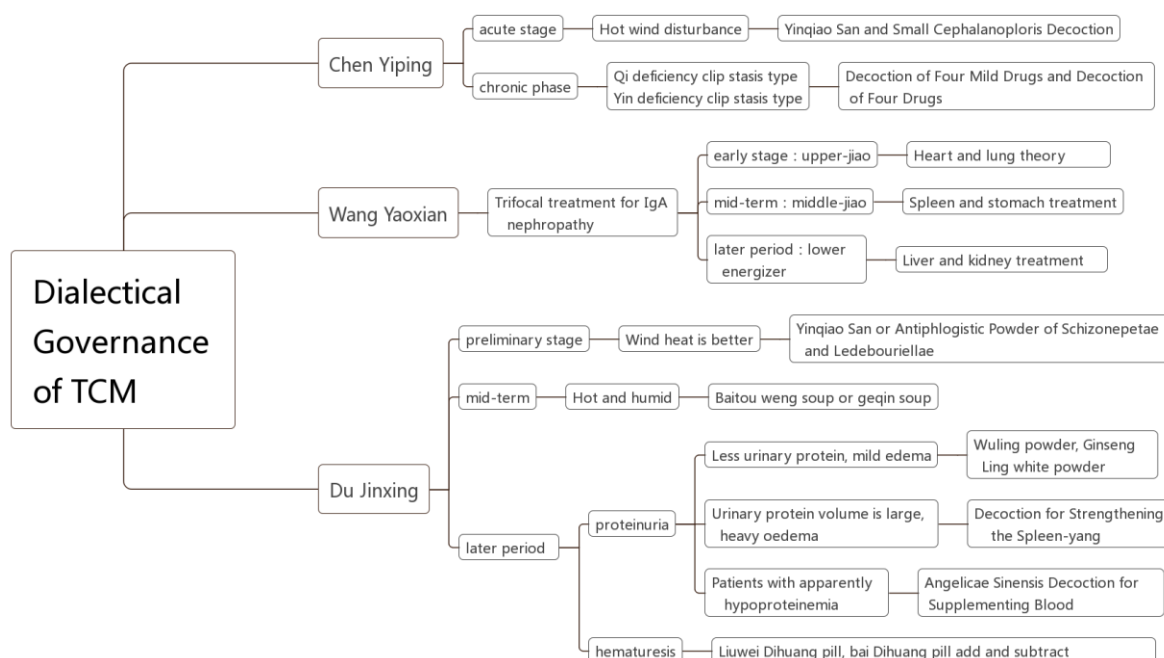


Figure 2: Dialectic treatment of IgA nephropathy in Traditional Chinese medicine

3. Knowledge of IgA nephropathy in Western medicine

IgA nephropathy is a kind of immunopathological reactive glomerular disease, also known as immune complex nephropathy. Its pathogenesis is related to immune system abnormalities, genetic factors and environmental factors. For example, see Figure 3, the specific pathogenesis is not fully defined, and further research is needed to explore its pathogenesis and treatment methods. In the course of treatment, various factors should be considered comprehensively, and comprehensive treatment methods should be adopted to achieve the optimal treatment effect.

3.1. Pathogenesis of IgA nephropathy

3.1.1. Immunological factors

The pathogenesis of IgA nephropathy is related to the deposition of immune complexes in the

renal glomeruli. IgA antibodies in IgA nephropathy patients bind to antigens to form immune complexes that are deposited within the glomerulus, leading to local inflammatory responses and damage in the glomerulus, eventually leading to glomerulosclerosis and impaired renal function. It is now believed that the core of IgAN is the deposition of IgA 1 in the mesangial region of the glomerulus, and leads to the proliferation of mesangial cells and increased mesangial matrix. Studies have shown that IgA deposited in the mesangial region of the glomerulus is poly IgA 1, and the level of poly IgA 1 in the serum of patients is also increased [9]. Recently, the results of various research methods have shown the abnormal glycosylation of IgA 1 molecules in IgAN patients, that is, the absence of O-galactose chain [10]. This galactose-deficient IgA 1 (Gd-IgA 1) is composed of either a terminal N-acetylgalactosamine (GalNAc) or sialate (GalNAc) [11]. The pathogenesis of IgA nephropathy is correlated with abnormalities of the immune system. IgA antibodies in patients with IgA nephropathy may be associated with the abnormal activities of immune cells such as B cells and T cells, leading to the dysregulation of the immune system and the weakened immunosuppressive function, thus promoting the occurrence of IgA deposition and glomerular injury. At present, it is generally believed that IgA nephropathy develops from "multiple strikes". The first blow refers to an increase in circulating IgA1 levels of abnormal O-glycosylation in the hinge region. These molecules lack Galactose (Galactose deficient IgA1, GdIgA1) in some O-glycans in the hinge region, so they are exposed to N-acetyl Galactosamine (GalNAc) as terminal glycans. The second hit the formation of diglycan specific IgG or IgA1 Autoantibody, targeting the end of the hinge region of Gd IgA1 containing GalNAc. The third hit refers to the formation of circulating immune complexes containing Gd IgA1 and IgG Autoantibody. The fourth blow refers to the entry of some circulating immune complexes into the mesangial area through the fenestra in the glomerular capillaries, causing mesangial cell proliferation and excessive production of extracellular matrix, cytokines, and chemokines, ultimately leading to chronic glomerular injury. Hyperactivation of T cells, especially Th 2, Th 17, Tfh and Th 22 subsets, plays an important role in the pathogenesis of IgA nephropathy. Th 2, Th 17, and Tfh-type interleukin contribute to the elevated synthesis of Gd-IgA 1, and Tfh cells can stimulate the production of anti-Gd-IgA 1 autoantibodies by IL-21. Meanwhile, Th 2, Th 17, Th 22, and Treg cells aggravated the glomerular damage in different forms of action.

3.1.2. Genetic factors

IgA nephropathy may be associated with variations in certain genes that may lead to abnormal production and deposition of IgA antibodies resulting to glomerular damage and impaired renal function. Many scholars believe that gene polymorphism may be related to the generation and development of IgA nephropathy, different genotypes of patients with their clinical manifestations or pathological types may also be different, and the disease may be related to a variety of genes such as renin angiotensin system gene polymorphism, uterosulin gene polymorphism, MBP polymorphism, cytokine polymorphism, TGF- β 1 gene polymorphism, etc. Studies [12] have shown that strong genetic factors in the pathogenesis of IgA nephropathy, and genes such as CFHR-5, TNFSF13, and IL-18608A / C are associated with the pathogenesis of IgA nephropathy. In addition, IL-1R1, IL 1-1R 2, MCP-1-2518, and CCR-2 + 190 are associated with the disease progression of IgA nephropathy. Domestic and foreign studies [13] also show that some biomarkers such as IgA with abnormal glycosylation in serum and urine, mannan-conjugated lectin (MBL), microRNA, neutrophil gelatinase-related apolipoprotein in serum and urine are helpful to evaluate the progression and prognosis of IgA nephropathy.

3.1.3. Environmental Factors

Environmental factors may also influence the occurrence and progression of IgA nephropathy. Some studies have shown that factors such as infection, diet, and environmental pollution may be related to the occurrence of IgA nephropathy, which may lead to the occurrence and development of IgA nephropathy by affecting the function of the immune system and glomeruli.

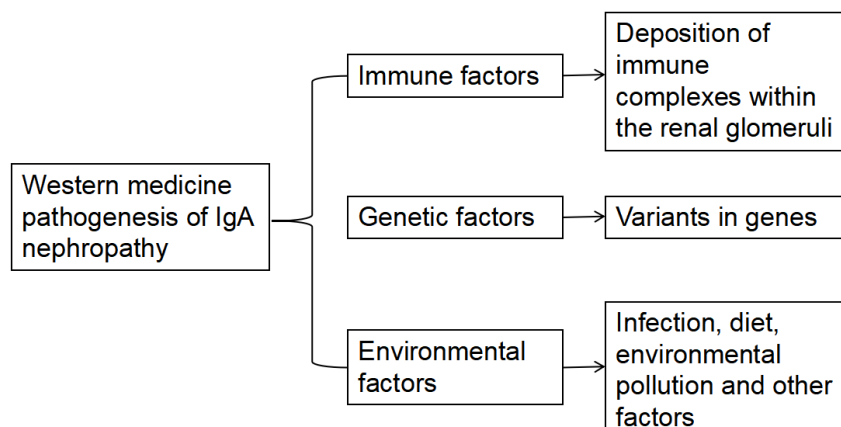


Figure 3: Western medicine pathogenesis of IgA nephropathy

3.2. Treatment of IgA nephropathy in Western medicine

The western medicine treatment measures of IgA nephropathy includes the following aspects, as shown in Table 2:

3.2.1. Control of hypertension

Hypertension is an important factor that accelerates glomerulosclerosis and promotes the deterioration of renal function. Hypertension is one of the common complications in patients with IgA nephropathy, and rational control of blood pressure can slow down glomerular injury and renal function decline. Commonly used antihypertensive drugs include ACEI, ARB, calcium channel blockers, etc. The efficacy of ACEI and ARB at home and abroad is the only recommended treatment in the KDIGO guidelines. PeiY class[14]Oxidative stress was decreased significantly with ACEIs; Cheng J et al. [15] suggested that ACEI / ARB combination was better than the use alone, and that ACEI / ARB had significant efficacy in reducing urinary protein and protecting renal function through a systematic evaluation of 11 ACEI / ARB patients for the treatment of IgA nephropathy RCTs.

3.2.2. Control of proteinuria

Proteinuria is one of the main symptoms in patients with IgA nephropathy, and controlling albuminuria can slow glomerular injury and decreased kidney function. Commonly used drugs include ACEI, ARB, tacrolimus, etc. 2016 latest edition of the Japanese Society of Nephrology (JSN)[16]ACEI or ARB is recommended for patients with proteinuria and stage 1-3 CKD above 1.0 g / d, for patients with proteinuria 0.5 to 1.0 g / d. Professor Wang Haiyan of China, et al. [17] suggested that for proteinuria in 0.5 g / dIgA, nephropathy patients, ACEI / ARB drugs can be the first choice, which can effectively reduce urinary protein and stabilize renal function in patients with IgA nephropathy, and set as grade A recommendation.

3.2.3. Immunosuppressive therapy

In patients with IgA nephropathy with severe kidney injury, immunosuppressive therapy can slow down disease progression and renal function decline. Commonly used immunosuppressive drugs include glucocorticoids, cyclophosphamide, methotrexate, etc. In IgA nephropathy, immunosuppressants such as glucocorticoids and cyclophosphamide can reduce or even stop the process of immune complex deposition at the glomerular site by reducing the ability of B cells to secrete antibodies, and then improve renal function and delay the disease process. Clinical general use of combined drugs, the effect is remarkable, Zhu Mingzhi et al. pointed out that [18]: glucocorticoids combined with cyclophosphamide and phenolic enzymes had good clinical results, and urine protein quantification, blood creatinine, urea, uric acid were significantly lower than that of glucocorticoid group alone. Wang Weiping believed that [19] patients with nephropathy refractory nephropathy syndrome as the main clinical manifestation, the results showed that the total response rate was 71.1%. Some patients' repeated renal biopsy showed reduced pathology, the degree of mesangial hyperplasia, and the strength of IgA granule deposition was weakened.

3.2.4. Other treatments

For patients with IgA nephropathy, anticoagulation, tonsillectomy and deep-sea fish oil can also be used. Other symptoms and complications in patients with IgA nephropathy require symptomatic supportive treatment. Such as anemia, hypoproteinemia, can use erythropoietin, plasma protein for treatment.

Table 2: Western medicine treatment of IgA nephropathy

Therapeutic measure	Specific drugs
Control of hypertension	commonly used antihypertensive drugs include ACEI, ARB, calcium channel blockers, etc.
Control albuminuria	commonly used drugs include ACEI, ARB, tacrolimus, etc.
Immunosuppressive therapy	commonly used immunosuppressive drugs include glucocorticoids, cyclophosphamide, methotrexate, etc.
Other treatments	Anticoagulation, tonsillectomy, and deep-sea fish oil application were used. Such as anemia, hypoproteinemia, can use erythropoietin, plasma protein for treatment.

4. Conclusions

In conclusion, IgA nephropathy is a common glomerular disease and its treatment involves multiple aspects of integrated OWM. According to traditional Chinese medicine, the pathogenesis of IgA nephropathy is mainly related to dampness-heat, phlegm turbidity internal resistance, spleen and kidney Yang deficiency, qi stagnation and blood stasis, etc. It is usually used to clear heat and dampness, tonifying kidney qi, promoting blood circulation, and regulating emotions. Moreover, some traditional Chinese medicines such as baicalensis, gardenia, Eucommia ulmoides, peach kernel and so on are often used in the treatment of IgA nephropathy. However, the western medicine pathogenesis of IgA nephropathy involves immune complex deposition, immune system abnormalities, genetic factors and environmental factors. Western medicine treatment measures include control of hypertension, proteinuria control, anticoagulation therapy, immunosuppressive therapy and symptomatic supportive therapy. However, dosage, compatibility and other factors, and there are toxic side effects and adverse reactions; the treatment of IgA nephropathy in Western medicine should avoid overuse of drugs and adverse reactions. The two need to make

comprehensive analysis and judgment according to the specific situation of the patient, adopt individualized treatment plan, and need long-term observation and evaluation of the treatment effect.

At present, the study of integrated Chinese and western medicine in the treatment of IgA nephropathy has been gradually strengthened. Some studies have shown that the combination of traditional Chinese medicine with western medicine can reduce the dose of western medicine, reduce the adverse reactions of western medicine, and can improve the therapeutic effect. For example, studies [20] show that the combination of traditional Chinese medicines such as baicalensis and gardenia with ACEI or ARB can significantly reduce proteinuria and blood pressure and improve renal function. At the same time, the combination of traditional Chinese medicine with immunosuppressants can reduce the dose of immunosuppressants, reduce the adverse reactions of immunosuppressants, and improve the therapeutic effect [21]. But the quality and reliability of these studies differ. In general, the research progress of the treatment of IgA nephropathy in Traditional Chinese and Western medicine has been gradually strengthened. The combination of traditional Chinese and western medicine can give full play to the advantages of both sides to maximize the treatment effect, providing more choices and ideas for the treatment of IgA nephropathy. At the same time, relevant research is needed to be further strengthened in order to better explore the advantages and potential of integrated Chinese and western medicine in the treatment of IgA nephropathy.

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