

Therapeutic Profile of IgA Nephropathy Regarding Pharyngeal Kidney Theory

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Abstract: *IgA nephropathy (IgAN) is the most common glomerular disease, which is one of the main causes of chronic kidney disease. The course of this disease is prolonged, and the condition is often recurrent, and most of the disease changes after respiratory, gastrointestinal, and urinary infections, and respiratory infections are the most common of the three, which makes the treatment more difficult. In Chinese medicine, there is no direct name for this disease, but according to its symptoms, it can be categorized as "hematuria", "edema", "urolithiasis", "slow kidney wind" and other diseases. The disease is often caused by the recurrence of exogenous infections. For the recurrence of this disease due to exogenous infection, Chinese medicine treats IgA nephropathy from the pharynx according to the theory of "pharyngeal and renal correlation", which has achieved good clinical efficacy, and this point of view has received more and more attention nowadays. This article focuses on the treatment of IgA nephropathy from the pharyngeal-renal theory.*

Keywords: IgA nephropathy, Pharyngeal kidney theory, Traditional Chinese medicine, Etiology and pathogenesis.

1. Etiology and Pathogenesis

1.1 Knowledge of the Etiology of IgA Nephropathy

In recent years, IgA Nephropathy has become a research hotspot, and more and more Chinese medicine doctors have expressed their unique views on the treatment of IgA Nephropathy, which also highlights the unique advantages of Chinese medicine in treating IgA Nephropathy. With the in-depth study of the disease, most of the doctors believe that the pathogenesis of IgA Nephropathy is mainly based on the deficiency of the root cause, in which the deficiency of qi and yin is the root cause, stasis of blood, dampness-heat and heat-toxicity are the key to the disease mechanism, and the external evils are the important causative factors for the disease; the location of the disease is in the kidney, and it is closely related to the lungs, the spleen, the liver, and the triple jiao. IgA Nephropathy is classified into the Chinese medicine category of "hematuria IgA nephropathy belongs to the category of "blood in urine", "turbidity in urine", "edema", "kidney wind" and "deficiency labor" in Chinese medicine. The "Theory of the Origin and Criteria of All Diseases" says: "If the wind enters the Shaoyin, then blood will be urinated. When the wind is outside, the throat is congested, the lung heat is forced down to the kidneys, and the kidneys are damaged, and the blood overflows out of the veins, resulting in blood in the urine." The source of all diseases - edema disease symptoms "cloud:" the kidney is the main water, the spleen and stomach are the main earth, earth gram water..... this stomach can not transfer water gas..... impregnation of the internal organs. Spleen get water wet gas..... spleen disease can not system water, so the water gas only to the kidney." Pointed out that edema disease is closely related to the kidney, spleen and stomach. Suwen - Taiyin Yangming theory: "injured in the wind, the upper first received; injured in the wet, the lower first received." Su Wen - Water-Heat Points Theory: "Kidney, the gate of the stomach is also unfavorable to close the door, so the water is gathered from its class." Jin Gui Yao Liao - five organs wind-cold accumulation disease pulse evidence and treatment" said: "heat in the lower jiao, then urine blood." Pointed out that dampness is the main

cause of kidney disease, dampness downstream, can be issued for edema, dampness into heat, burn the kidney, can be issued for blood in urine. From the above, we can see that the ancient medical doctors believe that this disease is mainly in the kidney, involving the lungs, spleen and stomach, the etiology of the disease is closely related to the wind, dampness, heat and other evils. Chinese medicine theory says that "kidney is the foundation of the innate nature" and "spleen is the foundation of the innate nature", the kidneys store the essence; the spleen is responsible for ascending and clearing, and is the main transporting and transforming. IgA nephropathy clinical symptoms in Chinese medicine can be categorized as The clinical symptoms of IgA nephropathy in Chinese medicine can be categorized as "blood in urine", "edema", "fatigue", "kidney wind" and so on, and the name of "kidney wind". IgA nephropathy is caused by the deficiency of the spleen and kidneys. IgA nephropathy is caused by spleen and kidney deficiency, which is caused by a variety of factors that deplete vital energy, such as congenital insufficiency, acquired dietary impurity, and internal injuries of seven emotions, triggering dysfunction of the body's immune system; triggered by external evils and injuries, resulting in recurring episodes of hematuria, and prolongation of the disease. Kidney is the foundation of the innate, the deficiency of the foundation of the innate, the spleen is the foundation of the innate, the foundation of the innate is not nourished, and the external evils from the mouth and nose, invading the lungs, so IgA nephropathy and lung, spleen and kidney organs are inseparable. Traditional Chinese medicine believes that the pathogenesis of IgA is characterized by a mixture of deficiency and solidity, and that the treatment of IgA should be based on supporting and replenishing the deficiency, supplemented by activating blood circulation and removing blood stasis [1]. Nie Lifang [2] summarized that the most common TCM syndromes of IgA nephropathy are qi and yin deficiency, liver and kidney yin deficiency, spleen and kidney qi deficiency, and spleen and kidney yang deficiency. Chen Xiangmei et al. [3] multicenter epidemiological survey of TCM syndromes in IgA nephropathy found that the most common standard syndromes were damp-heat syndromes and blood stasis syndromes, which accounted for 31.6% and

28.9% of the total, respectively. Recent studies have shown that the damp-heat syndrome accounts for 46.7% of the total number of morbidity syndromes in patients with IgA nephropathy [4]. And Wang Xinrong et al. [5] found that the severity of IgA nephropathy was significantly and positively correlated with damp-heat syndrome. The pathogenesis of dampness-heat syndrome is the internalization of dampness-heat due to the malfunction of the lung's transmission, the spleen's transportation, and the kidney's vaporization, or the deficiency of the lung, spleen, and kidney's qi, which makes it easy to feel dampness-heat external evils. Dampness for the disease, heavy turbid viscous, and dampness for the Yin evil, easy to attack the Yin position, the sense of entry, the first under the affected, the kidney is located in the lower Jiao, for the five viscera under the pole, more susceptible to it. To summarize, both IgA nephropathy or IgA nephropathy with symptoms are closely related to the lung, spleen and kidney, so this article from the lung, spleen and kidney on the treatment of IgA nephropathy dampness-heat certificate.

1.2 Western Medicine's Understanding of the Etiology and Pathogenesis of IgA Nephropathy

IgA nephropathy was first reported by Berger et al [6] in 1968, and is the most common primary glomerular disease worldwide. Its clinical manifestations are diverse, with mucosal infections followed by microscopic hematuria or asymptomatic hematuria with or without proteinuria as the main symptom, and accompanied by varying degrees of hypertension and renal impairment. IgA nephropathy is mainly dependent on renal biopsy puncture immunopathology for a definitive diagnosis, which is characterized by the following pathologies. The pathology is characterized by the deposition of IgA molecules in the glomerular mesangial area, with or without IgG and/or IgM deposits. At present, the pathogenesis of IgA nephropathy has not been clearly defined, and foreign scholars summarize it as a four-fold blow model: first, genetic or environmental factors lead to the production of galactose-deficient IgA1 (Gd-IgA1); second, the production of circulating antibodies specific for Gd-IgA1; third, the formation of pathogenic immune complexes containing Gd-IgA1; fourth, the pathogenic immune complexes pass through the glomerular endothelial cell window, deposited in the glomerular tunica, activating the complement pathway and initiating glomerular injury [7-8]. In recent years, research on the pathogenesis of IgA nephropathy has made great progress, and studies have shown that mucosal immune abnormalities may play an important role in the etiology of IgA nephropathy, and more studies have been done on respiratory mucosa, for example, there is a close relationship between inflammatory episodes of the tonsils and polyglottic hematuria [9]. In recent years, there have been many studies on the "intestinal-renal-related theory", in which mucosa-associated lymphoid tissues cause subclinical intestinal inflammation [10]. Smerud et al. [11] applied a new intestinal glucocorticoid, budesonide, to treat IgA nephropathy. The drug is released mainly in the ileocecal region of the intestinal tract and can precisely inhibit the local production of pathologic IgA, thus exerting therapeutic effects. In patients with IgA nephropathy accompanied by proteinuria, a 40% reduction in urinary protein was observed in patients after 6 months of treatment with this drug. Some

studies have also shown the role of B cells and complement in the pathogenesis of IgA nephropathy [12-13]. According to Zhang Yu, IgA nephropathy is characterized by deficiency of spleen and kidney, external wind is the causative factor, and ambient wind is the basic factor of IgA nephropathy [14]. Liu Baohou put forward the viewpoint of "if dampness and heat are not eliminated, protein is difficult to be eliminated", emphasizing that dampness and heat are the key causative factors of IgA nephropathy [15]. According to Wang Yulin, IgA nephropathy is characterized by deficiency of spleen and kidney, and dampness and blood stasis are the key factors. Protein is the essence of the human body, which is related to the production of the spleen and the sealing and storage of the kidney, and the deficiency of spleen and kidney results in the spillage of essence, so the consolidation of essence is the most important factor. [16]. Fan Yongsheng believes that IgA nephropathy is located in the kidney, and is related to the lungs, spleen, kidneys and the triple jiao. Hematuria is caused by the feeling of wind-heat, and the evil heat enters into the interior and turns into heat, which damages the veins and collaterals, depletes the heart's yin, and the heat is transferred to the small intestine, or the overwork is excessive, which damages the spleen's qi, and qi doesn't regulate the blood [17]. According to Huang Wenzheng, IgA nephropathy is related to the malfunction of spleen and kidney, and the unfavorable pivot mechanism of Shaoyang Sanjiao, and the interaction between external evils and ambient evils is the reason why the disease does not recover [18]. Li Jianmin believes that the internal cause of IgA nephropathy is due to congenital insufficiency, old age and body weakness, long time illness, labor and leisure, emotional and emotional disorders, dietary disorders and so on, while the external cause is mostly due to the feeling of external evils, and he firstly puts forward the theory of "stasis and paralysis of the kidney complex" in chronic kidney disease, which means that the kidney complex loses its nourishment after a long period of time, and the blood stasis, heat, dampness and toxicity are hidden in the kidneys. Paralysis of the kidney complex is more serious [19]. Zhu Bangxian believes that the pathogenesis of this disease for the qi lifting and lowering disorder, turbid and clear, visceral deficiency for this, the evil poison congestion for the symptom, the treatment of ascending and descending turbid, eliminating toxicity and transmitting the method of evil [20]. Kong Wei believes that this disease is a mixture of deficiency and reality, dampness and heat with stasis as the symptoms, spleen and kidney deficiency as the main cause, external sensation as the trigger, wind-heat under the compulsion for hematuria [21]. According to Ding Cherry, the main mechanism of IgA nephropathy is the deposition of "turbid toxin" in the kidneys, and the accumulation of dampness, heat and stasis in the kidneys, which is both the cause of the disease and the product of the pathology [22]. The medical doctors believe that the pathogenesis of IgA nephropathy is the deficiency of the standard, the deficiency of the lungs, spleen and kidneys, and the unfavorable qi of the triple jiao, and the standard for the wind, dampness, heat, stasis and other evils, the deficiency of positive qi, and the interaction of evils, which will lead to the onset of the disease.

2. Theoretical Basis of Chinese Medicine for "Pharyngeal and Kidney Related"

The Ling Shu - meridians and veins of other theories" has the

cloud: "kidney foot Shaoyin vein from the little finger under the..... Its straight from the kidneys up through the liver and diaphragm, into the lungs through the throat and clip the tongue this..... is the main kidney disease"; "Ling Shu - this transmission" cloud: "Shaoyang belongs to the kidneys, the kidneys are connected to the lungs, so will be the two viscera." The ulcer doctor Daquan" cloud "where the sore throat, are the disease of the lesser yin", "kidney water can not moisturize the throat, so it is also sick."; "the source of all diseases wait for". The "Essay on the Origin and Criteria of Various Diseases - The Criteria of Blood in Urine" said, "If the wind is in the Shaoyin, then there will be blood in the urine." The Complete Book of Sores and Ulcers Experience - Volume 1" states: "The throat should be weather is the system of the lungs." According to Chinese medicine theory, the throat belongs to the kidney, the system of the lungs, the lungs and the kidney meridians are connected and coherent, the five elements of gold and water, the lungs are gold, the kidneys are water, the lungs are the mother of the kidneys, the kidneys are the son of the lungs, the yin and yang of both nourish each other and replenish each other, the lungs are full of Yin and Yin and are transported to the kidneys, the kidneys are full of Yin and Yin and are nourished to the lungs, so that the kidney Yin is not dried up and the lungs are not in lack of fluids. If the patient externally affected by wind-heat evils, the knot throat, wind-heat evils from the pharynx through the meridian into the shaoyin kidney, resulting in kidney loss of sealing, essence and blood with urine out of the blood urine, as the "Yellow Emperor's Classic of Internal Medicine", said: "the wind evil in the shaoyin, then blood in the urine". Wind-heat evil long detained not to go, ambush in the Shaoyin, heat evil up burning in the pharynx can be seen throat pain, as the "Medical Zong Jinjian" pointed out that: "Shaoyin heat evil upward reversal, then passed through the place of no disease also." Kidney disease does not lead to recurrence or aggravation of the disease after a long period of time. Ren Jixue believes that the throat for the kidney, liver, stomach three veins of the main, the patient on both sides of the throat, the back wall of the veins stasis, showing red red or scarlet, or even red and swollen, for a long time, this is the poisonous evil entrenched in the throat, the long-term role of the kidney Palace. If the evil poison for a long time stasis is not in addition to the solution, the evil gas for a long time detained in the kidneys, depletion of kidney yin, yin deficiency phase fire delusion, false fire on the burn throat, such as the "Spiritual Pivot, the meridian" said: "is the Lord of the kidneys are sick..... pharyngeal swelling on the gas, aisle dry and pain." The Jingyue Encyclopedia" said: "the cause of deficiency evil, harm to the Shaoyin, the five organs are injured, the poor must be and kidney." Chronic kidney disease patients with chronic illness, blood, qi, yin and yang are all weak, unable to resist the exogenous evil invasion, the pharynx bears the brunt of the downward interference with the kidneys through the meridian, the poison must penetrate into the camp blood, immersed into the qi and liquid, by the kidney meridian, invasion of the kidneys; Kidney qi victimization, renal essence is injured, the kidney of the body for a long time with all the loss of [23]. It can be seen that the pharynx and the kidney in the physiological interconnection, in the pathology of each other, the two have a close connection, so there is a "pharynx kidney related" theory. Pharynx and kidney in the body through the meridians are closely linked to each other, the evil attack on the surface, through the meridians can enter

the kidney, kidney blood damage, physical damage, there can be hematuria, urine, edema and other clinical manifestations. This disease is mostly chronic, the classics have a cloud: long illness will be weak, the evil gas is easy to get together, so the patient in the external evil disturbances, often see the recurrence and aggravation of the disease. On the pharynx and kidney close connection between the two as early as in the "Nei Jing" that is, "Ling Shu" said: "..... is the main kidney disease, hot mouth and dry tongue, pharyngeal swelling on the gas, the quarrel dry and pain"; "Typhoid - identify the Shaoyin disease pulse evidence and treatment" in the cloud: "Shaoyin disease two or three years, the evil Qi easy to get together, so patients often see the recurrence of the disease and aggravation when there are external evil disturbances. "Shaoyin disease two or three days, pharyngeal pain, with licorice soup, not bad, with tangerine stems soup; Shaoyin disease, pharyngeal injuries, sores, can not speak, the sound does not come out of the person, the bitter wine soup main; Shaoyin disease, pharyngeal pain, half-summer loose and soup main". This shows that the pharynx, the relationship between the two kidneys is quite close. The pharynx as the gateway to the lungs, often as the first place to suffer from evil when attacked by foreign evil, foreign evil can be congested in the throat, mother and child disease, the internal shed in the kidneys, so the condition can be seen repeatedly and aggravated. A study on the main clinical manifestations of IgA nephropathy [24] also pointed out that hematuria, proteinuria, lumbago, sore throat, edema, fatigue, cough, dry mouth, dry throat are the main clinical manifestations of the disease, in which, in addition to the manifestations of the renal system, the performance of the throat accounted for a considerable proportion.

3. Pathogenesis of the "Pharyngeal-kidney Related" Theory in Chinese Medicine

Regarding the pathogenesis of this disease, the pharynx is the organ of diet, breathing and voice, connected to the oral cavity, connected to the lungs and stomach, and the key to the circulation of the meridians. The pharynx is the system of the lungs and belongs to the kidneys. Spiritual Pivot - meridians and veins," said: "kidney foot Shaoyin vein, from the little finger under the..... Its straight, from the kidneys up through the liver and diaphragm, into the lungs through the throat clip tongue this..... is the main kidney disease, hot mouth and dry tongue, pharyngeal swelling on the gas, yelp dry and pain." Therefore, the pharynx to kidney meridian Qi moistening, physiological function is normal, then not for the evil offender. Kidney qi, blood, yin and yang imbalance can cause throat diseases, and throat diseases can be transmitted to the kidney through the meridian. It can be seen that pharynx and kidney are closely related in function and disease. Evil and poison enter from the airway and end up in the pharynx, and the poison follows the Shaoyin meridians down to violate the membrane and blood of the kidney, resulting in kidney disease. It is now believed that the external evil is one of the important causes of this disease [6] [25]. Most of the patients with this disease have evidence of deficiency of internal organs, and the body's inability to prevent evil is easy to attract exogenous evil, and the exogenous evil is wind as the first, mixed with other evils, and the larynx is often the first to be affected by it. Throat and kidney to meridian connection, external evil attack throat can be transmitted directly to the

kidney through the meridian, at the same time, gold and water, mother disease and child, the kidney is damaged, essence is not solid, water and wetness is not transformed, then the patient appeared to hematuria, urinary turbidity, edema as a representative of the performance. In addition, if the positive qi is deficient and unable to drive away the evil, the exogenous evil will stay in the kidney complex for a long time, and it will be easy to generate the ambient evil over a long period of time. Vulnerable evil blocked in the kidney, qi, blood and fluid operation is not smooth, over time into dampness, blood stasis "poison" evil [7] [26]. In all kinds of chronic kidney diseases, the occurrence of renal fibrosis, an important pathological process, in Chinese medicine can be the scope of the obstruction in the kidney, Liu Shangjian et al. [8] [27] believe that the exogenous evil and internal "poison" is an important pathogenic factor in the obstruction in the kidney.

4. A Modern Account of the Theory of "Pharyngeal and Renal Correlation".

Although the pathogenesis of IgA is not yet completely clear in western medicine, but at this stage, it is more recognized as the "multi-strike theory", in which mucosal immunity plays an important role in the occurrence and development of Ig A nephropathy [28]. The current study [29] believes that when patients have upper respiratory tract infection and/or tonsillitis, it will activate the abnormal immune response of mucosa, which can lead to the abnormal expression of ST6 gal NAc-II, and then Gd-Ig A1 secretion through IL-6 and IL-4; in addition, when respiratory mucosa is stimulated (especially tonsil mucosa), it will lead to the high expression of TLR9, which can increase Gd-Ig A1 secretion, and patients with Ig AN have a high level of TLR9 expression, and Gd-Ig A1 secretion [31]. In addition, when the respiratory mucosa is stimulated (especially the tonsil mucosa), TLR9 will be highly expressed, resulting in the secretion of Gd-Ig A1, and the immune complexes deposited in the thylakoid membrane area of patients with Ig AN will be the abnormally secreted Gd-Ig A1. In addition, Wyatt et al. [30] also put forward the concept of the mucous membrane-bone marrow axis, and a large number of detailed studies have been carried out by subsequent scholars on the basis of this hypothesis. The small amount of IgA produced by the respiratory mucosa can be transferred to the bone marrow, where it proliferates and is released into the bloodstream, and finally deposited in the glomerular mesangial zone, leading to the development of the disease. According to its location and function, the respiratory mucosa can belong to the category of Chinese medicine's guardian surface, which is the main body of the lungs, and the larynx is the gateway of the lungs [32]; the abnormal proliferation of immune complexes is located in the bone marrow, which is the main body of the kidneys, which coincides with the theory of Chinese medicine's "laryngeal and renal correlation". As an autoimmune nephropathy, the pathogenesis of IgA nephropathy has not yet been fully clarified. The "multi-strike theory" [33] due to immunoregulatory disorders is currently an internationally recognized theory: genetic or environmental factors related to galactose-deficient IgA1 (Gd-IgA1) circulating levels are elevated; a large amount of Gd-IgA1 as an autoantigen activates the immune response and stimulates the B cells to react with the IgA nephropathy. Activation of immune

response, stimulation of B cell differentiation into plasma cells and production of anti-Gd-IgA1 autoantibodies; formation of pathogenic immune complexes containing Gd-IgA; deposition of immune complexes in the glomerular mesangial area, which triggers inflammatory reactions, stimulates proliferation of mesangial cells and extramembranous stroma aggregation, and ultimately leads to glomerulosclerosis and interstitial fibrosis. The deposition of IgA1-based immune complexes is central to the pathogenesis of IgAN, therefore, as the main site for the production and secretion of large amounts of IgA molecules in the body [34], mucosa-associated lymphoid tissue (MALT), especially gut-associated lymphoid tissue (GALT) and nasopharyngeal-associated lymphoid tissue (NALT) are thought to be associated with IgA1 and IgAN. NALT) are thought to be strongly associated with IgA nephropathy [35]. Evidence suggests that mucosal immune abnormalities due to persistent antigenic stimulation play an important role in the development of IgA nephropathy, and that respiratory or gastrointestinal mucosal infections in patients with IgAN are often accompanied by worsening hematuria and proteinuria. [36,37,38] The results of the GWAS genome-wide association study at [39] show that several IgAN susceptibility genes are associated with the maintenance of the intestinal mucosal barrier and the regulation of mucosal immune responses, and that perturbation of the immunological pathway generated by intestinal IgA is a key factor in the development of IgA nephropathy. Perturbation of the intestinal IgA-generated immune pathway is a core defect in IgAN pathogenesis. Currently, treatments targeting the regulation of mucosal immune abnormalities, such as tonsillectomy [40] and budesonide capsules [41], have become a hotspot and a new direction in the prevention and treatment of IgAN.

5. Modern Research in TCM on Pharynx and IgAN

There is no standardized criteria for the diagnosis of IgAN. According to its clinical symptoms and signs, the diagnosis is closely related to the four organs of the liver, spleen, lungs and kidneys, and involves factors such as external evils, qi, blood, yin and yang. Different scholars hold different views on the dialectic of treating IgAN from the pharynx, and there is a lack of standardized and objective dialectic. Peiqing Zhang [42] classified IgAN into wind-heat syndrome, kidney yin deficiency syndrome, and kidney yin deficiency with wind-heat syndrome according to its clinical symptoms. Wang Gang [43] The diagnosis of IgAN is based on 3 types: heat in the throat, spleen deficiency with dampness and heat, and kidney deficiency with dampness and stasis. Zhan Yongli [44] The dialectic of IgA nephropathy from the pharyngeal viewpoint is divided into 3 types: lung qi deficiency, heat and toxin disturbing the pharynx, spleen qi weakness, heat and evil guest pharynx, and kidney yin deficiency, residual heat remaining in the pharynx. Practical Guidelines for TCM Diagnosis and Classification of IgAN [45] is classified into wind-heat syndrome of exogenous sensation, damp-heat syndrome of the lower Jiao, lung and spleen qi deficiency, qi and yin deficiency, liver and kidney yin deficiency, and spleen and kidney yang deficiency according to the acute exacerbation period and the clinical remission period. According to Chinese medicine theory, the wind-heat evil enters from the mouth and nose, and then accumulates in the

throat, disturbing the kidneys through the meridian, the essence of the material is lost, and the blood overflows out of the veins, so proteinuria, hematuria, accompanied by burning pain in the throat; prolonged illness is not resolved, or the evil is detained in the kidneys for a long time, which depletes the yin of the kidneys, and the inflammation of the deficiency burns the pharynx, which results in the slight pain and dryness in the throat, suggesting that the actual evidence of the pharyngeal pain of the IgAN patients is based on the heat knotting of the throat, and the deficiency of the kidney and kidney yin is deficient in the deficiency. The treatment of IgAN is to clear heat and detoxify the pharynx, while the deficiency is to nourish yin and nourish the pharynx. The treatment principles of IgAN vary slightly from doctor to doctor. Zou Yanqin adopts the two major treatments of "clearing heat and nourishing yin and pharynx" according to the deficiency and realities of the disease [46]. Shao Zhaodi's treatment of this disease is based on nourishing yin, benefiting the kidney and strengthening the spleen, and at the same time flexibly utilizing the dispelling of wind and clearing heat to benefit the pharynx, etc., to differentiate between the symptoms and the urgency of the disease, and to treat the symptoms and the root cause together [47]. Nie Lifang summarized the treatment of IgAN and found that nourishing qi and yin was the most frequently used treatment, most of which was combined with heat-clearing and detoxification therapy, and established the method of nourishing qi and kidney according to the core of the pathogenesis of IgAN, which is deficiency of qi and yin. [48-49]. Zhan Yongli [44], on the other hand, focuses on clearing heat and detoxifying the pharynx, as well as benefiting the qi, strengthening the spleen and nourishing the yin. Fan Yongsheng [50] believes that the pathogenesis of IgA nephropathy is complex and prolonged, so the treatment of acute exacerbation should be to relieve the epidermis and promote the lung, dredge the wind and benefit the pharynx, while the chronic prolongation of the disease should be to benefit qi and consolidate the epidermis, strengthen the spleen and nourish the kidney. For the sore throat caused by IgAN with deficiency of qi and yin, Li Wenwen et al. [51] used a self-proposed formula (Astragalus, Radix Salviae Miltiorrhizae, Chasteberry, Radix Aristolochiae, Radix et Rhizoma Gastrodiae, Radix et Rhizoma Gastrodiae, Radix et Rhizoma Genus, Radix et Rhizoma Genus, Radix et Rhizoma Ophiopogonis, Glycyrrhiza Uralensis, Platycodonis, Cicada Shells, Stiffworms) to treat the sore throat. Wang Xinhui et al. [52] observed the clinical effectiveness of Yiqi Nourishing Yin and Pharyngeal Formula (Sheng Huangqi, Huang Jing, Honeysuckle, Lotus Leaf, Su Ye, Cicada Shell, Han Fang Ji) combined with Pharyngeal Pecking Treatment for IgAN patients with pharyngitis symptoms, and the results of the study showed that the Yiqi Nourishing Yin and Pharyngeal Formula could effectively reduce hematuria and sick improve the symptoms of pharyngeal discomfort in IgAN patients. Wang Jiming et al. [53] explored the clinical efficacy of the self-proposed compound formula Jian Kidney Kang (honeysuckle, buckwheat, platycodon, cocos root, raw astragalus, wolfberry, artichoke, Chinese yam, Job's tears, Poria cocos, Rhizoma Ligusticum Chuanxiong, motherwort, hyssop, leucaena leucaena, psoriasis, psoriasis) in the treatment of IgAN, and the results showed that the compound formula Jian Kidney Kang can significantly improve the clinical symptoms of patients with IgAN with the clinical

effectiveness of total effective rate reaching 88.33%. Based on the theory of "treating from the pharynx", Li Siping et al. [54] prepared a traditional Chinese medicine compound formula (Yinhua, forsythia, cicadas, Xuanshen, Scutellaria baicalensis, Paeonia lactiflora, Thornybirdia, Stipendula, and Baihua snakesnake tongue grass) with the functions of clearing heat and removing toxins and dispersing wind and evils, which showed that the treatment significantly reduced the symptoms of pharyngolaryngeal pain and hematuria of the observation group, and the adverse reactions were lower than those of the control group. Du Anmin [55] et al. treated IgAN directly from the pharynx, and based on the scripture formula, they formulated their own compound formula with the effects of clearing the pharynx and relieving the throat, cooling the blood and stopping bleeding (Thorny mustard, honeysuckle, forsythia, radix et rhizoma, red peony, XuanShen, Zedoary, stibnis, cicadellia, Scutellariae barbatae, Radix scutellariae, Cynomolium leucocephalum, Cynomorium albidum), and the result showed that it helped to improve the laboratory indexes such as the 24-hour urinary protein quantification, urinary red blood cell count and other laboratory indexes, and the therapeutic effect was obvious. The above basic and clinical studies show that the identification and treatment of IgAN involves the pharynx and kidney, and the clinical treatment and medication mainly focuses on clearing heat and removing toxins to benefit the pharynx, nourishing yin and tonifying the kidney to nourish the pharynx, which suggests that the pharynx has a close relationship with the occurrence and progression of IgAN.

6. Modern Medical Research on Pharynx and IgAN

The pathogenesis of IgAN has not been completely clarified so far. Some studies have found that IgAN is triggered or aggravated by upper respiratory tract mucosal infections, especially pharyngitis and tonsillitis [56], about 62.3% of patients with IgAN have chronic pharyngitis, which accounts for the highest proportion of IgAN patients, and about 32.8% are accompanied by chronic tonsillitis [51]. Patients with IgAN usually present with hematuria or aggravation of the original condition within 72 h after upper respiratory tract infections, suggesting that chronic throat inflammation is an important trigger and aggravating factor for IgAN development. This suggests that chronic pharyngeal inflammation is an important causative factor in the development and exacerbation of IgAN [57]. Therefore, improving pharyngeal inflammation in IgAN patients is an effective way to control the occurrence or exacerbation of IgAN at the source. Tonsil is a peripheral immune organ with a large number of crypts and lymphocyte infiltration, and its crypts increase the chances of contact with external antigens, and antigens repeatedly stimulate the B cells on the surface of the tonsil to produce a large number of IgA immune complexes, which are deposited in the glomerular mesangial area and cause IgA nephropathy. Therefore, some scholars' observational studies have found that removal of the tonsil can reduce the IgA immune complexes in the blood serum, reduce recurrence, and improve the Clinical efficacy of IgAN [58]. Yang et al. [59] randomized patients with renal biopsy pathology clearly diagnosed as IgAN into a conventional drug treatment group and a tonsillectomy combined with conventional drug treatment group, and the results showed

that the tonsillectomy group had better efficacy, with a reduced relapse rate and an increased remission rate. A nationwide multicenter randomized controlled study in Japan found that tonsillectomy combined with glucocorticoid therapy for IgAN after tonsillectomy had significant efficacy in reducing urinary proteins, thereby protecting the kidneys and delaying the progression of renal function. Liu et al. [60] included 14 cohort studies (1,431 patients) on the efficacy of tonsillectomy for IgAN in a meta-analysis, and the results showed that tonsillectomy combined with hormone therapy was superior to hormone therapy alone, and the patients' disease progressed to the stage of ES. The results showed that tonsillectomy combined with hormone therapy was superior to hormone therapy alone, and the rate of progression to ESRD decreased. Duan et al. [61] included 19 meta-analyses (3,483 patients) on the long-term efficacy of tonsillectomy in IgAN, which also proved that tonsillectomy could help to slow down the progression of renal function and reduce the incidence of ESRD. Adachi et al. [62] examined the efficacy of tonsillectomy for IgA nephropathy, and concluded that the combination of hormone shock therapy with tonsillectomy was the most effective way for IgAN to be treated. Adachi et al. studied the efficacy of tonsillectomy after IgA nephropathy and concluded that tonsillectomy combined with hormone shock therapy is an effective treatment for IgA nephropathy, and that hormones should be used before or after tonsillectomy. However, some scholars hold a negative attitude towards tonsillectomy in patients with IgA nephropathy, suggesting that tonsillectomy is not effective in reducing the recurrence of IgA nephropathy and slowing down the progression of renal function [63]. Since the above included literature are non-randomized controlled trials, whether tonsillectomy can effectively reduce the recurrence rate of IgAN and slow down the progression of renal function still needs to be further verified by large-sample, higher-quality randomized controlled trials, which can provide an evidence-based basis for clinical treatment.

7. Summary

Clinical control of the inflammatory state of IgAN patients, especially the pharyngeal infection foci, can actively improve the inflammatory state of the kidneys and improve the therapeutic effect of patients. It is of great significance to avoid triggering or aggravating renal diseases. The treatment of chronic nephritis from the pharynx provides new ideas and methods for clinical treatment. In recent years, active control of inflammatory foci of infection has received more and more attention, but the shortcomings are that most of them are single-center, small-sample clinical observations and summaries, and the treatment modalities and medications are diversified in different places, and there is no uniform standard for related indexes: such as pharyngeal symptoms, observation indexes, exclusion criteria, and efficacy criteria of patients with IgAN, and so on. There is a lack of large-sample, multi-center, randomized and double-blind clinical studies, low level of impact factor of evidence-based medicine, and no relevant animal experiments, which makes it difficult to promote its application on a large scale. In the future research, we should gradually strengthen the understanding of the etiology and pathogenesis of patients with chronic nephritis with pharyngeal symptoms and the identification of the law, improve the standards; conduct multi-center, large-sample,

randomized double-blind controlled clinical studies, and then explore the mechanism of traditional Chinese medicine for the treatment of chronic nephritis with pharyngeal infections through animal experiments, pharmacological studies, to develop precise and effective special formulas and special medicines to lay a good clinical foundation. However, it is regrettable that in many experiments, most of the research subjects are recurrent hematuria, or simple hematuria, or a small amount of proteinuria, suggesting that the pathological damage is relatively light, so whether the removal of tonsils or the treatment of pharyngeal inflammation is applicable to a variety of pathological damage and the degree of pathological damage of chronic nephritis needs to be further researched and explored. Clinically, IgAN has a high incidence, long course, recurrent attacks, and prolonged recovery, which affects the quality of life and prognosis of patients to a certain extent. Based on the theory of "pharyngeal and renal correlation", this paper organizes, summarizes, and collates the relevant literature from the theory of meridians and internal organs, modern research in Chinese medicine, and modern medicine in Western medicine, which is of great significance in the clinical prevention and treatment of IgAN. In this regard, future research on the prevention and treatment of IgA nephropathy from the theory of pharyngeal and renal organs should collect relevant data, summarize the dialectical methods and diagnostic and therapeutic rules through the database, and establish objective and standardized dialectical methods and diagnostic and therapeutic norms, so as to give full play to the strengths of traditional medicine; explore the pharmacological effects of the components of traditional Chinese medicine prescriptions and their interconnections, and apply the research methods of cyber-pharmacology to elaborate the pharmacological effects of traditional Chinese medicine prescriptions from the aspects of multi-targets, multi-pathways and so on. The research method of network pharmacology will be applied to elaborate the mechanism of IgA nephropathy by Chinese herbal medicine compound; meanwhile, high quality, large sample, multi-center randomized controlled clinical trials will be conducted to provide evidence-based basis for the prevention and treatment of IgA nephropathy in the future.

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