

Research Progress of Traditional Chinese Medicine in the Treatment of Lupus Nephritis

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Abstract: The progress of Chinese medicine treatment of lupus nephritis in recent years is reviewed from the aspects of etiology and clinical treatment, focusing on the clinical treatment from the three aspects of diagnosis and treatment, specialized prescription treatment, and the combination of Chinese and Western medicine, and the existing problems and the direction of efforts are put forward.

1. Introduction

Lupus nephritis (LN) is one of the autoimmune inflammatory damages with multi-system involvement caused by systemic lupus erythematosus (SLE), and it is the most common and important visceral complication, which is the main cause of death in SLE patients [1]. The 10-year renal survival rate of patients is 81%-98%. Among the patients, 50%-80% have the clinical manifestations of lupus nephritis, and on general pathologic examination, 90% of the patients have renal involvement, and combined with electron microscopy and immunofluorescence, 100% of the patients have different degrees of renal lesions [1]. In recent years, with the national support for the cause of traditional Chinese medicine, the effect of traditional Chinese medicine in the treatment of lupus nephritis has been remarkable in recent years. Based on the concept of "unity of man and nature" and "holistic diagnosis" of traditional Chinese medicine, traditional Chinese medicine treatment of this disease has the advantages of holistic conditioning, multi-system and multi-target interventions, as well as reducing the side effects and dependence of drugs. At the same time, it reduces the side effects and dependence of drugs and delays the occurrence of complications. Therefore, the progress of Chinese medicine research on this disease in recent years is summarized as follows.

2. Etiological Factors and Pathogenesis

2.1. Modern Medical

Immune complex (IC) is formed by the binding of pathogenic autoantibodies and corresponding antigens, mainly including circulating immune complexes and in situ immune complexes. IC

lesions are recognized as the fundamental pathogenesis of LN. In SLE patients, cell apoptosis is disrupted, self tolerance is lost, and the cell clearance system is dysfunctional, leading to the accumulation of various autoantibodies and free nucleosomes in the body, resulting in the formation of a large amount of IC and deposition in the kidney [2], as shown in Figure 1.

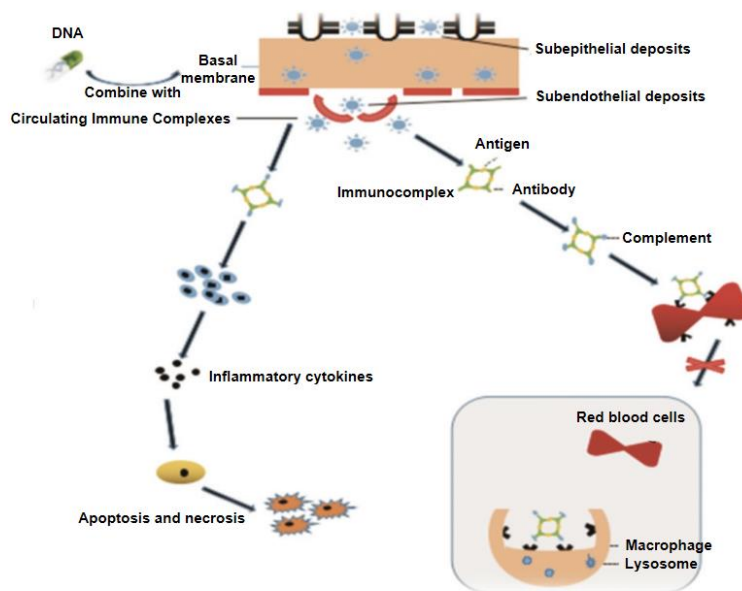


Figure 1: The pathological mechanism of Lupus nephritis

2.2. Traditional Chinese Medicine

Du Xiulan et al. [3] believed that the etiology of this disease is mostly due to the lack of congenital inspection and illumination, or internal injury of seven emotions, overwork, resulting in liver and kidney deficiencies, yin deficiency, fire, and feel the wind, dampness, and heat, especially wind-heat and toxicity to take advantage of the weakness into the interior, and the combination of fire and stasis blockage of the meridians, Pan burns the camping blood, depletion of yin and fluid, and heat and toxicity within the injury and spleen and kidneys and the onset of the disease. Jin Miaowen [4] believes that this disease is based on yin deficiency, and its long-standing root lies in the yin deficiency of the liver and kidney, yin deficiency for a long time, transforming heat into wind, and the evils of the disease for a long time, stasis and toxicity into the complexes, which can lead to qi and yin deficiency in a long time, and later on, the spleen and kidney deficiencies. B deca is the same source, resides in the lower jiao, the kidney is the water house, easy to suffer from dampness, the liver is a wooden organ, easy to generate wind, and the blood is the main drain, easy to block the blood and generate blood stasis. Zhu Yueling [5] believed that lupus nephritis patients due to congenital endowment deficiency, or post-disease physical weakness, or heat and toxicity dampness invasion of the body burns the kidney, kidney Yin deficiency, meridian stasis, dampness and stagnation due to the intersection of obstruction. Dampness and stagnation accumulate in the kidney complex, and the kidney complex is damaged. This leads to the loss of kidney essence and the loss of essence and blood substances, resulting in edema, proteinuria, hematuria and so on. Therefore, kidney deficiency, dampness obstruction and blood stasis are the main pathogenesis of lupus nephritis.

3. Chinese medicine treatment

3.1. Identification and treatment

Du Xiulan's Qingre Jiedu Decoction [3] was often used in the early stages of LN, with the treatment mainly focusing on clearing heat, relieving toxin and eliminating evil. The clinical manifestations of this syndrome type included fever, erythema on the face or toes, edema of both lower limbs, proteinuria or/and hematuria, etc. The therapy for spleen and kidney yang deficiency syndrome type of LN was mainly to tonify the spleen and kidney, warm yang and promote blood circulation, promote water and dampness, which was treated with modified Zhenwu Decoction. This prescription included *atractylodes macrocephala*, *poria cocos*, *rehmannia glutinosa*, *paeonia lactiflora*, *astragalus membranaceus*, *polygala tenuifolia*, *alisma orientalis*, *cuscuta* seed, fried leech and roasted licorice. The clinical manifestations of spleen and kidney yang deficiency syndrome type included edema in the lower limbs or whole body, lumbar debility, aversion to cold, urinary protein can not subside for a long time or accompanied with hypoproteinemia, etc. Spleen deficiency with reverse ascending of stomach-qi syndrome type manifested as abdominal distension, dyspnea and cough, nausea and vomiting, mental fatigue, etc. The therapy for this syndrome type was mainly to strengthen the spleen and lower the adverse flow of qi, which was treated with modified Xiao Chaihu Decoction. And this prescription was based on Xiao Bianxia Decoction and added with *pinellia ternata*, *poria cocos*, *Magnolia officinalis*, *rhizoma atractylodis macrocephalae*, *rhizoma alismatis*, *radix scrophulariae*, etc. Fang Qi et al. [6] believed that the treatment for noxious heat syndrome type should be clearing heat, relieving toxin, cooling blood and eliminating spots. It can be treated with modified Wuwei Xiaodu Beverage and Xijiao Dihuang Decoction. Yin deficiency and internal heat syndrome type should be treated with modified Zhibai Dihuang Pill and Xijiao Dihuang Decoction, which aimed to nourish yin, clear heat, cool blood and promote blood circulation. For Yin deficiency of the liver and kidney, nourishing the liver and kidney, cooling the Blood and activating the Blood were the treatment methods. In cases of deficiency of both qi and yin, the treatment is to nourish qi and nourish yin by adding or subtracting Si Jun Zi Tang and Er Zhi Wan.

Shi's [7] clinical diagnosis is often divided into four types: heat and toxin incandescence type, mostly seen in the acute active stage, symptoms: high fever, bleeding tendency is obvious, such as subcutaneous petechiae, epistaxis, blood in urine, irritability, like to drink, or even fainting and delirium or convulsions, or joints are red and swollen and painful, the tongue is reddish-red, and the pulse is flooding and counting. Treatment should be to clear heat, remove toxins and cool blood, the formula is Rhinoceros Jiao Di Huang Tang combined with Wu Wei Sterilizing Drink with additive subtractions. Liver and kidney yin deficiency and qi and yin deficiency are commonly seen in the subacute or chronic stage of the disease. Liver and kidney yin deficiency is characterized by dryness of the eyes, warmth of the hands, feet and heart, dryness of the mouth with a desire to drink, low-grade fever and night sweating, and dryness and knotting of the stools. The treatment should nourish the liver and kidney, activate blood circulation, and clear the blood, and the formula should be Qui Shao Di Huang Tang plus subtractions; the type of qi and yin deficiency has the deficiency of qi, such as tiredness, laziness and laziness, bad wind and easy to catch a cold, and also has the deficiency of yin, such as heat of the hands, feet and heart, night sweating, and dryness of the mouth and throat, or there are symptoms of qi deficiency and yin deficiency intermingled with the symptoms of bad wind, fear of cold and heat of the hands, feet and heart, dryness of the mouth and lack of desire for water, and dryness of the stools at first, followed by scanty stools, etc. The treatment should benefit the qi and nourish the yin and the formula should be Sen. The treatment should benefit the qi and nourish the yin, and the formula is Senqi Di Huang Tang or Dajian Yuan

Decoction with additions and subtractions. Spleen and kidney deficiencies are mostly seen in the chronic stage of the disease, and those who favor spleen and kidney qi deficiencies have symptoms such as generalized fatigue, lack of warmth of the limbs, soreness and weakness of the waist and knees, little food and abdominal distension, loose stools, and a moist and big or fat tongue with teeth marks on the side. Treatment should strengthen the spleen and benefit the kidney, the prescription is to replenish the middle and benefit the qi soup or heterogeneous gongsan plus cuscuta, golden cherry seeds, bone marrow, or use the five son diffraction zong pill plus dangshen ginseng, astragalus; if the spleen and kidney yang deficiency, the evidence of coldness and limb cold, edema is serious, the treatment should be warm and replenish the spleen and kidneys, the prescription is to use the real spleen drink or real wu soup with subtractions. Li Wei [8] and others believe that the common types of clinical symptoms of LN are: (1) Heat and toxicity blazing syndrome: high fever that does not go away, thirst and coldness, agitation and restlessness, or even fainting and delirium, erythema on the face and skin, bright red, epistaxis and urination, or red, swollen and hot pain in joints, with a reddish-red tongue or purplish-dark tongue, yellow moss, and a rapid pulse or number of strings. The treatment should be clearing heat and removing toxins, cooling blood and dispersing blood stasis, and the formula is to add subtraction of Clear Plague and Toxin Drink. (2) Yin deficiency internal heat syndrome: symptoms of flushing, erythema hidden, dry throat and mouth, five heart heat, lumbar and knee soreness and weakness, or persistent low fever, zygomatic redness and night sweating, dizziness and tinnitus, urinating red dry stools, red tongue with little fur, pulse is thin and countless. The treatment should be nourishing yin and lowering fire, cooling the blood and detoxifying the toxin, and the formula should be Zhi Bai Di Huang Tang combined with Artemisia Phellodendron Botrytis Soup. Symptoms include fatigue, shortness of breath, laziness, self-sweating, night sweating, dry mouth and pharynx, heartburn, or low-grade fever, with red tongue, little or thin moss, and fine or weak pulse. The treatment should benefit the qi and nourish the yin, and the formula should be Ginseng Astragali Di Huang Tang plus subtractions. (3) Deficiency of spleen and kidney: symptoms include fatigue, lumbar and knee soreness and weakness, low appetite and abdominal distension, fear of cold and cold limbs, loose stools and clear urine, or generalized edema, swelling below the waist, with pale and fat tongue with teeth marks, white and greasy moss, and fine pulse. Treatment should strengthen the spleen and benefit the kidney, activate blood and promote water retention, the formula selected ginseng ling bai ju san alloy scarcity kidney qi pill plus subtractions.

Xiao [9] divided into 5 cases of heat and toxicity, Yin deficiency and internal heat, Yin deficiency of liver and kidney, Qi and Yin deficiency, and Yang deficiency of spleen and kidney, respectively, and treated 21 cases with the addition and subtraction of clearing the plague and defeating the toxin, Zhi Bai Di Huang Wan, Liu Wei Di Huang Wan, Wu Zi Diffractive Pill, Sijunzi Tang combined with Wu Zi Diffractive Pill, and Right Angelica Pill, with the result of 16 cases of obvious effect, 12 cases of improvement, and 3 cases of ineffectiveness. Wu [10] and others believed that lupus nephritis manifested as renal syndrome identified as spleen and kidney yang deficiency, spleen and kidney qi deficiency, yin deficiency, dampness and heat syndrome, and he used Zhenwu Tang, Ginseng Lingbaijushu San, Er Zhi Wan, Dazhongyin Pill with additions and subtractions to treat each of these syndromes separately, and he gave each formula must be added with centipede, white flower snakeskin Tongue Grass, Snake Bed Seeds, Semen Ziziphroxyton, sour jujube nuts and other medicines for activation of blood and elimination of blood stasis. As for patients with renal failure, he added rheum officinale and oysters to remove dampness and turbidity, supplemented with medicines for tonifying qi and nourishing blood, nourishing yin and reducing fire. The result was 25 cases of complete relief, 37 cases of significant relief, 14 cases of partial relief, 41 cases of ineffective, with a total effective rate of 95%. Chen [11] believes that heat and toxicity, spleen and kidney Yang deficiency, Yin deficiency, internal heat, Qi deficiency and blood

stasis are the most common patterns.

3.2. Specialized treatment

Huang Shang [12] and others concluded that Ning Kidney, Dispelling Dampness and Eliminating Stasis Soup is an empirical formula for the treatment of lupus nephritis, which mainly consists of Radix Rehmanniae Praeparata, Rhizoma Ophiopogonis, Radix et Rhizoma Dryis, Radix et Rhizoma Momordica, Radix Achyranthis Bidentatae, Radix Bupleurum Suffruticosum, Radix et Rhizoma Polygoni Multiflori, Rhizoma Atractylodis Macrocephalae, Radix Cardamomum, and Semen Mucilaginae, which work together to nourish the kidney, dispelling dampness and eliminating stasis. By nourishing kidney yin and supporting positive qi, it is conducive to the clearing and dispersal of dampness-heat and blood stasis; promoting dampness is conducive to the restoration of kidney yin; dispelling blood stasis makes the water and qi flow; nourishing the kidney, promoting dampness and dispelling blood stasis complement each other. This proves that Ning Kidney Dispelling Dampness and Residual Blood Stasis Tang can significantly reduce the incidence of urinary protein and thus reduce nephritis. Lin Ning [13] and others believed that the addition of Artemisia sinensis and turtle shell soup could inhibit the expression of Th17 cells in MRL/lpr lupus mice and improve the active pathological changes of their kidney tissues. Huang Chuanbing [14] et al. combined the theory of traditional Chinese medicine with years of clinical practice and summarized Qiqi Huang Strengthening the Spleen and Nourishing the Kidney Granules. In the formula, Astragalus tonifies qi, strengthens the spleen, diuresis and reduces swelling, while Radix Rehmanniae Praeparata benefits the kidney and fills in the marrow, tonifies blood and nourishes yin. Yam tonifies the yin of the spleen and kidney; Atractylodes macrocephala and Poria strengthen the spleen and support the earth, and promote diuresis and seepage of dampness. Golden Cherry, Raspberry and Semen Cuscutae are used to nourish the liver and kidneys, strengthen the spleen and kidneys, consolidate essence and shrink urine, and are used as adjuvant herbs. The combination of all the drugs, nourishing the spleen and kidney, benefiting qi and nourishing yin is the main method, supporting the positive and repelling the evil, tonifying and benefiting with clearing and benefiting, taking into account both the symptoms and the root cause, and cooperating with western medicines to act on the kidneys, which can regulate the immune system, lower the urinary proteins, and protect the kidneys and detoxification. Qu Huanru [15] found that the treatment plan of tonifying kidney and consolidating essence formula combined with high-dose astragalus injection could not only reduce the quantitative amount of 24h urinary protein of the patients, down-regulate the activity index of lupus, and reduce the occurrence of infections, but also increase the ratio of CD4+, CD25+, and Treg cells to a certain degree, reduce the level of IL-17, and improve the immune disorder of the patients. Correcting the immune status not only helps to stabilize the condition, but also effectively prevents the occurrence of infections and enhances the patients' tolerance to hormone and immunosuppressant treatments.

4. Combined treatment of Chinese and Western medicine

Shen Jun [16] observed the ginseng and astragalus four-snake soup with raw astragalus, tai zi ginseng as the ruler, accompanied by fried atractylodes macrocephala, cornelian cherry altogether to help replenish qi and nourish yin, benefit the kidneys and strengthen the spleen, kidney qi is sufficient, spleen qi is healthy, qi and blood yin and yang are harmonized, then the positive qi is strong, and the elimination of evils out of the house. At the same time, Wu Zui Snake, Fang Feng and Cicada Shell were used to dispel wind and invigorate collaterals, while Qing Feng Teng, Bai Hua Snake Tongue Grass, Snake Berry, Snake Bed Seed and Plantain Grass were used to clear heat and promote dampness in order to get rid of the real evils of wind, dampness, heat and blood stasis,

so as to treat both symptoms and symptoms at the same time. It was also confirmed that the combination of western medicines with Senqi Si Snake Soup Plus and Minus formula in treating patients with mildly and moderately active lupus nephritis could reduce urinary protein, improve serum albumin, stabilize renal function, and improve immune indexes, and it could improve the Chinese medicine syndromes of the patients more effectively. It can more effectively increase the rate of patients' Chinese medicine symptoms, reduce clinical symptoms, and has better clinical safety. Ye Rengao [17] classified lupus nephritis into four types: heat and toxicity blazing type, liver and kidney yin deficiency type, yin deficiency internal heat type, spleen and kidney yang deficiency type. He believed that the dosage of prednisone and cyclophosphamide was supposed to be increased in the early stages of the disease. Based on the theory "Yang is often enough, yin is often in deficiency", he adopted Xijiao Dihuang Pill and Qingre Jiedu Decoction to clear heat and relieve toxin, cool blood and promote fluid production. In the remission period, the patient's fever subsided, and the main contradiction was internal heat and yin deficiency, with unclear prognosis. The treatment was transformed to nourishing yin and clearing heat, while applying cyclophosphamide. For leukopenia, drugs that can benefit qi and nourish blood were adopted, such as astragalus membranaceus, angelica sinensis, ginseng, etc. During the stable period, the dosage of cyclophosphamide and prednisone should be reduced. And the prescription should be Liuwei Dihuang Pill and Zuogui Pill, mainly to tonify the liver and kidney. Nie Ailing [11] divided lupus nephritis into heat and toxicity blazing, yin deficiency and blood deficiency, qi and yin two injuries, evil heat injury to the liver, kidney yin deficiency, spleen and kidney yang deficiency six types of treatment. A total of 51 patients were treated with the combination of hormone, cyclophosphamide and trastuzumab tablets, and the total effective rate is 88.2%.

5. Conclusion

In summary, in recent years, Chinese medicine treatment has achieved obvious results, especially the combination of TCM evidence and disease identification, which has unique advantages in relieving symptoms, improving efficacy, reducing recurrence and side effects of western drugs, etc. However, there are also some problems, such as: no unified identification and typing pattern and efficacy assessment standards, lack of correlation studies between TCM evidence and pathology, immune indexes, etc. In response to these shortcomings, we should carry out LN diagnosis and treatment and laboratory indicators. In view of these shortcomings, we should carry out research on the correlation between LN diagnosis and treatment and laboratory indexes and renal pathology, so as to make the diagnosis and treatment objective and more targeted, and make full use of modern science and technology to increase the basic experimental research, and strive to elucidate the mechanism of traditional Chinese medicine from the cellular and molecular level.

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