

A study on Chinese Medicine to alleviate the Adverse Effects of Western Medicine in the Treatment of Lupus Nephritis

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Abstract: *Lupus nephritis (LN) is the most serious and common complication of systemic lupus erythematosus (SLE), which is mainly treated with glucocorticoids combined with immunosuppressive drugs, but its long-term use in large quantities can produce many toxic side effects, which seriously affect the continued application of therapeutic drugs and affect the prognosis and quality of life of patients. TCM can effectively reduce the toxic side effects of western drugs, improve clinical efficacy, reduce comorbidities, ensure the continued use of western drugs, reduce the relapse rate after discontinuation of drugs, and improve the prognosis of patients through evidence-based treatment. The combination of Chinese and Western medicine can effectively control LN activity, relieve symptoms, improve renal function, and reduce the side effects of Western medicine.*

Keywords: Lupus nephritis, Adverse reactions, Traditional Chinese Medicine.

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multisystemic damage accompanied by the formation of multiple autoantibodies [1]. 7-31% of patients have systemic lupus erythematosus nephritis (LN) at the time of SLE diagnosis, and 31-48% develop LN after SLE diagnosis, mostly within 5 years [2]. Clinical manifestations include fever, butterfly-shaped erythema on the face, rash, mucosal ulcers and photosensitivity, etc. It may even involve several organs or systems such as kidney, cardiovascular, blood, etc. When it involves the kidneys, it often manifests as hematuria, edema, hypertension, and even renal function impairment. Western medicine in the treatment of glucocorticoids (referred to as hormones) combined with immunosuppressants or biological agents, but will produce many toxic side effects, the near-term will appear excessive sweating, irritability, panic, sleep disorders, and other adverse reactions, the long-term effects mainly include a decline in the body's immune function, secondary infections, gastrointestinal bleeding, osteoporosis, diabetes mellitus, etc., so that the patient's compliance is poor, and the premature discontinuation of medication leads to the patient's relapse rate Higher. TCM has certain advantages in the treatment of LN. The combination of TCM's evidence-based treatment and prescription and medication on the basis of Western medical treatment has the advantage of reducing the toxicity and increasing the efficacy compared with the treatment of Western medical treatment alone, so that the remission rate of the treatment and the maintenance of the remission rate of LN can be significantly improved.

2. TCM's Understanding of LN

LN is a complex disease with many symptoms, which is categorized as "yin and yang toxicity", "kidney wind toxicity", "red butterfly sores", "edema", etc. [3], which is caused by the external attack of heat and toxicity due to the lack of innate endowment, diet and fatigue, seven emotions and internal

injuries. "and other disease categories, due to the lack of innate endowment, diet and fatigue, seven emotions, such as internal injuries caused by heat and toxicity of the external invasion of the evil, depletion of yin and blood, disturbing the balance of yin and yang, damage to the internal organs and meridians, qi and blood imbalance, so hair this disease. According to Bian Tianyu [4], this disease is characterized by kidney deficiency, with heat-toxin stasis as the symptom of the disease. Li Lili [5] and others emphasized that LN is caused by a combination of exogenous and internal injuries due to the lack of innate endowment, a combination of exogenous and internal injuries, a prolonged accumulation of evils and toxins, dampness, heat, and stasis as the symptoms, and the interplay of successive innate factors, with a deficiency of the essence and a deficiency of the mark and a mixture of emptiness and solidity in the course of the pathology. Although the pathogenesis of LN is intricate and complex, it always belongs to the underlying deficiency, with kidney deficiency being the main cause of the underlying deficiency, and the underlying reality being the inter-conjunction of heat and toxin, blood stasis, and dampness and turbidity, which contribute to the activity of lupus, with heat and toxin being the most important ones.

3. LN and Western Medicin

The pathogenesis of LN has not been fully elucidated, and it has been found that its main pathogenic mechanism is the activation of the complement system caused by the deposition of immune complexes in the kidney; the complement cascade reaction in renal tissues is caused by the deposition of immune complexes, which contributes to the proliferation and activation of glomerular thylakoid cells and release of a variety of inflammatory factors; autoantibodies of the kidneys form immune complexes that are deposited in the kidneys, and this can also lead to renal injury [6]. The target treatment for LN is at least 25% reduction in urinary protein within 3 months from the start of treatment, more than 50% reduction in urinary protein at six months, and complete remission at

one year, i.e., urinary protein <0.5 g/24h or random urinary UPCR <500 mg/g [2]. The majority of patients achieve remission within one year of treatment, and some patients require more than one year to achieve remission. Current therapeutic drugs for LN are mainly hormones, hydroxychloroquine sulfate, immunosuppressants, and biologics [7], of which hydroxychloroquine sulfate is the basic treatment, and hormones are the main drugs used in LN treatment for their powerful anti-inflammatory and immunosuppressive effects. Hormones mainly achieve therapeutic effects by reducing T lymphocytes, monocytes and eosinophils, decreasing the ability of immunoglobulin to bind cell surface receptors, inhibiting interleukin production and release, thus decreasing the conversion of T lymphocytes into lymphoblastoid cells, and decreasing the concentration of complement components and immunoglobulin [8]. The selection of immunosuppressants is mainly based on the type of renal pathology and disease activity, and combined with other extra-renal lesions. Common clinical immunosuppressants mainly include cyclophosphamide, mertiomacrophenol ester, azathioprine, and calmodulin neural phosphatase inhibitors (cyclosporine, tacrolimus), etc., which interferes with the body's metabolic pathways in different ways to carry out immunosuppressive effects [9].

4. Traditional Chinese Medicine to Improve Efficacy and Alleviate Adverse Effects of Hormones

Chinese medicine believes that hormone is pure yang products, in the early stage of LN need a large number of hormone impact, making exogenous hormone in the body a large number of increase, depletion of the human body's "strong fire", "strong fire food gas" to "strong fire of the gas decline The "strong fire eating qi" leads to "the decline of the qi of the strong fire", which depletes the kidney qi and essence of the human body, resulting in exuberant fire and injury to the yin, which leads to the appearance of mental exuberance, flushed face and ears, dry mouth and fear of heat, red pharynx and tongue descending and other yin deficiency and hyperactivity of yang. In the stage of hormone reduction, due to the initial period of a large number of hormone impact after the heat and yin, yin exhaustion and injury to qi, qi and yin deficiency, the patient manifested as dry mouth and throat, upset and irritability, red tongue with little moss, pulse thin and number of symptoms, it should be clearing the heat and removing toxins, benefiting the qi and nourishing yin for the method, the formula is used in the treatment of the pulse of life powder plus subtractions. To the hormone maintenance stage, due to the long-term administration of hormones, resulting in the body's yin deficiency and yang, the symptoms of yin and yang deficiency, liver and kidney deficiency, the patient often appears to be fatigue, less breath and laziness, fear of cold limbs, lumbar and knee soreness and weakness, pale tongue, white moss, weak pulse, should be tonifying liver and kidney for the method, the formula selected right return pill plus reduction treatment [10]. Chinese medicine is involved in all stages of hormone withdrawal and reduction through evidence-based treatment, which can alleviate the adverse symptoms produced by hormones at different stages, accelerate the withdrawal of hormones, prevent the recurrence of the disease, and play its role of increasing efficiency and reducing toxicity.

Zhao Zhenxia [11] et al. randomly divided 127 lupus patients into a control group treated with hormone therapy and an observation group with the addition of the Chinese medicine Right Angelica Drink Plus Reduction on the basis of the control group, and found that creatinine, urea nitrogen, and the quantitative amount of 24h urinary protein of the observation group were significantly lower than those of the control group after 4 weeks of treatment ($P<0.05$). Guo Feng [12] et al. observed clinical SLE patients, the control group was given prednisone and hydroxychloroquine sulfate treatment, and the observation group added lupus static granules on top of it, and found that after 3 months of treatment, the reduction of Chinese medicine evidence points, SLE disease activity score, left atrial internal diameter, interventricular wall thickness, and left ventricular posterior wall thickness of the observation group was higher than that of the control group, and the efficacy of the combination of western medicine and lupus static granules in the treatment of SLE was remarkable. The efficacy of western medicine combined with lupus jing granules in treating SLE is remarkable, the patients' clinical symptoms are relieved more obviously, the degree of cardiac damage is reduced significantly, and the adverse reactions caused by hormone therapy can be reduced to a large extent, and the effect of increasing efficiency and decreasing toxicity is remarkable. Song Ke [13] et al. randomly divided 90 cases of LN patients into a control group that used conventional western medicines for symptomatic treatment, and the observation group added Si Miao Yong An Tang on its basis, and found that the levels of urea nitrogen and creatinine and the incidence of adverse reactions of the patients in the observation group were much lower than those of the control group after 3 months of treatment. Therefore, the above study can confirm that the participation of Chinese medicine can effectively improve the clinical symptoms of SLE patients, reduce the damage of renal function, reduce the adverse reactions produced by hormones, and improve the clinical efficacy.

4.1 Infection

Infection is an important cause of mortality in patients with LN, and its incidence is about 50% [14], bacterial infection is the most common, followed by viral and fungal infections, and the upper respiratory tract is the most common site of infection, which increases the recurrence rate of the disease, and seriously affects the patient's prognosis and the quality of survival. Sun Xin [15] et al. conducted a systematic study on the risk factors of concurrent infections in LN patients at home and abroad through Meta analysis and found that the risk factors for the occurrence of infections were mainly related to age, the dosage of immunosuppressants and hormones, the content of complement, the score of SLE activity, the number of organs involved and C-reactive protein. Among them, the long-term use of hormones can reduce the body's immunity, while the use of immunosuppressants can lead to leukopenia, thus inducing infections. Several studies have found that the intervention of TCM can effectively reduce the risk of infection and the number of recurrences in LN patients. Wang Li [16] et al. randomly divided 52 patients with LN into a control group given cyclophosphamide and prednisone treatment, and an experimental group to which the Yi Kidney Resolving Blood Stasis and Transmitting Evil Formula was added, and found that the infection rate of the

experimental group was significantly lower than that of the control group after 6 months of treatment ($P < 0.05$). Chen Yiming [17] et al. investigated the mechanism of action of Liuweidihuangwan in the treatment of lupus nephritis through network pharmacology and molecular docking technology, and found that there are multiple pharmacologically active ingredients in Liuweidihuangwan that can exert their therapeutic effects on LN and prevention of infection by acting on multiple target proteins. Studies have confirmed that the active ingredients of Liuweidihuangwan for the treatment of LN mainly contain quercetin, kaempferol, diosgeninogen, and sterol. Among them, kaempferol can enhance the inhibitory function of regulatory T cells (Tregs), which was found to increase the level of forkhead box P3 expression of Tregs and reduce PIM1-mediated phosphorylation of FOXP3 by S422 through animal experiments in rats, thus preventing a series of inflammatory disease infections from occurring. In conclusion, the occurrence of infections is mainly caused by intrinsic immunodeficiency and extrinsic immunosuppressive treatment, while the intervention of TCM can effectively prevent the occurrence of infections, reduce the number of disease recurrence and improve the quality of life of patients.

4.2 Immunocompromised

Hormones, as the basic medicine for the treatment of lupus nephritis, have a powerful immunosuppressive effect, and long-term use in large quantities will lead to low immunity of the patient, which will lead to a variety of other diseases. Xiao Jing [18] et al. summarized the experience of Prof. Wu Jinyu and found that Prof. Wu made good use of allopathic medicine to treat LN with remarkable efficacy, especially allopathic medicine Astragalus and Angelica to counteract the adverse effects of leukopenia caused by western medicines, Wu believed that Astragalus is the key medicine for treating LN, which is not only able to replenish the vitality of qi and blood, but also diuretic to eliminate edema, and to reduce the amount of urinary proteins, and the study found that: Astragalus is able to enhance the immunity of the human body, and to promote the growth and regeneration of cells. Research has found that astragalus can enhance human immunity, promote cell growth and regeneration, increase erythrocyte specific volume, and promote the proliferation and differentiation of hematopoietic stem cells. Angelica sinensis is an important medicine in blood, not only can replenish blood to improve the patient's anemia, but also can activate blood pain relief joint pain, but also can reduce hematuria, modern pharmacology found that it can elevate peripheral blood erythrocytes to promote hematopoiesis, inhibit platelet aggregation, to prevent thrombosis, vasodilatation, improve blood flow, and enhance the immune function of the body's role.

4.3 Osteoporosis

Osteoporosis occurs as a systemic metabolic disease caused by a decrease in bone density and bone mass, which increases the risk of fracture and destruction of bone microstructure. Many factors can cause osteoporosis in patients with LN, its own osteoblasts and osteoclasts balance state dysregulation, disorder, activated T lymphocytes produce and express a variety of cytokines and substances, vasculitis, microthrombosis caused by microcirculation obstacles to

reduce the local blood supply to the bone and lead to loss of bone mineral, anti-double-stranded DNA antibody can induce human monocytes to produce interleukin, $TNF-\alpha$, $IFN-\gamma$ and other pro-inflammatory factors, which aggravate bone destruction, etc. are all causes of osteoporosis [19]. Zhao Guisheng [20] et al. found that the bone density of lumbar spine and femoral neck were significantly lower than before treatment by observing 60 patients with LN who received low-dose hormone therapy for 12 months. Hormones are the drugs of choice for the treatment of lupus nephritis, the dosage is high and needs to be maintained for a long period of time. Osteoporosis is one of the main side effects of long-term hormone application, and it is also an important factor that affects the quality of survival of patients.

Chinese medicine believes that the long-term use of large amounts of hormones easy to make the human body yang depletion, kidney loss of sealing, kidney essence deficiency, there is no enrichment of the bones, bone hollow loss of nourishment and lead to osteoporosis, the "Chinese and Western confluence of the Essence of Medical Scripture," said: "the kidneys hide the essence of the essence of the essence of the medulla oblongata, medulla oblongata, the bones of the kidneys contained; medulla oblongata, the kidneys born of the essence of the essence of the essence of the medulla, medulla, medulla, medulla, the bones of the bone is strong enough!" and so on [21]. It can be seen that the TCM pathogenesis of osteoporosis is mainly kidney deficiency. Wang Dong [22] by observing 32 cases of SLE kidney yin deficiency type patients, take their own before and after the control method, in the original oral hormone treatment based on the addition of flavored Sanhuanguoben Tang, after 3 months of treatment to determine the patient's femoral neck bone mineral density, the results found that after 3 months of taking traditional Chinese medicine treatment, the patient's bone mineral density test results were significantly higher than the bone mineral density test results before taking traditional Chinese medicine, the traditional Chinese medicine can be used to prevent osteoporosis after taking hormone in SLE patients by increasing the patient's bone density Chinese medicine can prevent the occurrence of osteoporosis in SLE patients after taking hormones by increasing the patients' bone mineral density.

5. Chinese Medicine to Alleviate the Adverse Effects of Immunosuppressants

Before the introduction of hormones, the 5-year survival rate of LN patients was 44%, but the combination of hormones and immunosuppressive agents increased to 80% in the 1980s, and now to 90% [23], and the use of immunosuppressive energizers is effective in controlling the disease activity and mitigating the adverse effects, such as osteoporosis and infections caused by a large number of hormones, and it is the current routine use of medication in the treatment of the disease [24]. Treatment protocols should comply with individualized novel immunosuppressive regimens and promote multi-targeted therapies to improve LN treatment efficiency and long-term renal survival [25]. However, long-term use also produces many side effects. The toxic side effects of immunosuppressants are mainly nephrotoxicity, bone marrow suppression, liver damage, hematopoietic stem cell reduction, sharp decrease in the number of lymphocytes

in the peripheral blood, and impaired microcirculation, which lead to serious sequelae and even death from complications, while the involvement of Chinese medicine can effectively play a role in increasing the effectiveness and decreasing the toxicity and improve the quality of life of patients.

Zhong Qicheng [26] observed 64 patients with LN by randomly dividing them into a control group given hormone and immunosuppressant treatments, and a treatment group added Yiqiang Shengxue Tang on top of the control group, and found that the efficacy of the treatment group and the laboratory indexes (WBC, RBC, HGB, and PLT) were better than those of the control group after 3 months of treatment, and that Yisui Shengxue Tang was better than that of the control group in the treatment of the immune disorders due to the use of immunosuppressant with toxic side effects and blood system damage due to the use of immunosuppressants has a better curative effect. Shen Jun [27] observed 33 clinical patients, the control group was given hormone and immunosuppressant treatment, and the observation group added ginsengqi four snakes soup plus and minus formula on the basis of it, and found that after 12 weeks of treatment, the quantitative 24h urinary protein, the degree of decrease of Cr, and the degree of increase of ALB of the observation group patients were better than that of the control group, and the combination of ginsengqi four snakes soup plus and minus formula with western medicine can effectively improve the clinical symptoms of the patients and reduce the toxic and side effects of the western medicines. The combination of western medicine treatment with the formula of Ginseng Astragali and Four Snakes Soup Plus and Minus can effectively improve the clinical symptoms of patients and reduce the toxic side effects of western medicine. Wang Zhihua [28] by observing clinical LN patients, the control group was given hormone therapy, the treatment group was given lingdan tablets with Chinese herbal soup and a small amount of hormones and immunosuppressants, after the treatment, it was found that the improvement of clinical symptoms and laboratory indexes (blood sedimentation, urinary proteins, urea nitrogen and creatinine) of the treatment group was significantly better than that of the control group, and in the aspect of the western medication side effects, the patients of the treatment group experienced upper gastrointestinal bleeding, Coxsackie's sign, femoral head necrosis, gastrointestinal reactions and other adverse reactions were significantly lower than those in the control group.

6. Conclusion

In summary, LN remains a therapeutically challenging chronic disease due to its complex pathogenesis. With more and more clinical studies, more effective drugs and therapeutic regimens are being used in the clinical management of LN. Traditional Chinese medicine (TCM) is an important part of LN treatment, and a large number of clinical studies have confirmed that the involvement of TCM can effectively alleviate the clinical symptoms of LN, improve the laboratory indexes such as complement, blood sedimentation, urinary protein, creatinine, etc., and delay the progression of renal function damage. At the same time, TCM intervention can alleviate the adverse reactions caused by western drugs, such as infection, osteoporosis, immunocompromise, bone marrow suppression, liver damage,

etc. Because of the obvious side effects of western drugs, not only does it increase the pain of the patients, but also some of the patients can't even adhere to the treatment, which leads to the recurrence of the disease. In the course of LN treatment, hormones and immunosuppressant side effects mainly harm the body's positive qi, resulting in the body's yin and yang bias or deficiency. By treating its side effects with TCM evidence-based therapy, adjusting the body's qi, blood, yin and yang, supporting the positive and dispelling the evil, it not only reduces its clinical symptoms, but also plays a synergistic role with western medicines, which improves the patient's compliance and shortens the treatment cycle. The combination of Chinese and Western medicine in the treatment of LN, with their complementary advantages, not only helps to control the activity of the disease and improve the therapeutic efficacy, but also reduces the side effects of pure Western medicine and lowers the recurrence rate, which is worthy of extensive clinical promotion and application.

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