

# Research Progress in the Treatment of Idiopathic Membranous Nephropathy with Traditional Chinese Medicine

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**Abstract:** *Idiopathic membranous nephropathy (IMN) is an autoimmune disease and is the main cause of nephrotic syndrome. At present, there are many controversies about the means and effect of clinical treatment of IMN. Combined with cyclophosphamide and hormone, as the first-line treatment regimen for IMN, have obvious toxic and side effects, while calcineurin inhibitor, as the initial alternative treatment regimen, although it can effectively improve the clinical manifestations of IMN proteinuria and so on, it has a high degree of nephrotoxicity. In recent years, the TCM treatment of IMN has made great clinical achievements. TCM treatment follows the principle of "overall concept, syndrome differentiation and treatment", and adopts the characteristic therapy of internal and external treatment, which can effectively alleviate the refractory symptoms of IMN and has a good application prospect. To this end, this paper collected the literature data related to TCM treatment of IMN in recent years, and summarized the etiology and pathogenesis of IMN and TCM treatment of IMN, in order to provide a reliable basis for TCM treatment of IMN.*

**Keywords:** Traditional Chinese medicine, Idiopathic membranous nephropathy, Etiology and pathogenesis, Treatment.

## 1. Introduction

Idiopathic membranous nephropathy (IMN), a class of autoimmune diseases of unknown etiology, is the more common type of idiopathic glomerular disease [1]. Relevant studies have confirmed that the occurrence and development of IMN may be related to inflammatory mediators, genetics, humoral immunity and other factors, with proteinuria, edema, hyperlipidemia and other nephrotic syndromes as typical characteristics [2-5]. Epidemiological statistics show that the prevalence rate of IMN is about 24.9% in China, accounting for 24.9% of glomerular diseases. Prevalence rate of IMN is about 24.9% in China, accounting for 24.9% of glomerular diseases, and the proportion of IMN shows a significant upward trend [6]. Western medicine is the main treatment for IMN in clinical treatment. Cyclophosphamide combined with hormone and calcineurin inhibitors are commonly used for IMN treatment. However, clinical practice has proved that Western medicine has many toxic side effects and adverse reactions in IMN treatment, and the clinical therapeutic effect is not ideal, and there are problems such as repeated attacks after symptom relief. In recent years, Chinese medicine has made remarkable achievements in the data of IMN treatment and its complications. On the premise of clarifying the etiology and pathogenesis of IMN, following the principles of Chinese medicine treatment can effectively slow down the disease course of IMN patients and improve their clinical symptoms. To this end, the relevant progress of TCM treatment of IMN in recent years is collected and summarized, hoping to provide reliable ideas for TCM treatment of IMN.

## 2. Etiology and Pathogenesis

IMN has no related disease name in the field of Chinese medicine, combined with the clinical manifestations of the disease can be included in the category of Chinese medicine "edema", "exhaustion" and other diseases. Primary deficiency

with excess and intermixed deficiency are the etiology and pathogenesis of IMN. The syndrome differentiation can be divided into primary deficiency -- spleen and kidney deficiency, spleen and kidney deficiency, qi and Yin deficiency. Standard excess -- internal blockage of blood stasis, internal stopping of water and dampness, interjunction of dampness and stasis.

Combined with the typical clinical manifestations of IMN (edema, proteinuria, hematuria), the etiology and pathogenesis of IMN were discussed. Gan Anping et al. [7] believed that IMN was based on deficiency of lung, spleen and kidney, and was associated with wind, dampness, heat and blood stasis, among which "blood stasis" ran through the onset and development of IMN, and believed that ben-deficiency was the main pathogenesis of the disease. Wang Lin et al. [8] found that spleen-kidney deficiency was the pathogenesis of IMN by digging the medication rules of Professor Yang Hongtao in the treatment of IMN, and external wind, dampness turbidity, blood stasis and internal wind were the main causes of IMN. Chen Honglin et al. [9] pointed out in the analysis of medication used by Professor Song Liquan in the treatment of membranous nephropathy that IMN belonged to the syndrome of deficiency of the essence and deficiency of the spleen and kidney, namely the origin and phlegm-dampness and blood stasis. The deficiency of spleen and kidney, and the obstructed transport of fluid and fluid will form phlegm-dampness blood stasis, so the clinical manifestations are edema, proteinuria and hematuria. At the same time, due to phlegm-dampness block, blood stasis blocks the transport and nourishment of qi, blood and body fluid, making the patient's condition more serious. To this end, Professor Song Liquan clearly pointed out in the study that regulating the spleen and kidney, regulating the qi mechanism and repairing the physiological function of three jiao are important links in the treatment of IMN. Zhao Qihan et al. [10] summarized the pathogenesis of IMN as external evil and

internal deficiency. External evil is wind evil and internal deficiency is spleen-kidney Yang deficiency. Wind evil enters the body, Wei Yang deficiency can not compete with it, the evil enters the lungs can not operate normally and the spleen is dysfunctional, the circulation of blood, liquid, qi and liquid is blocked, resulting in blood stasis block and Yang deficiency block, so the spleen kidney Yang deficiency syndrome is the basic pathogenesis of IMN. With the deepening of the research on the etiology and pathogenesis of IMN in traditional Chinese medicine, the etiology and pathogenesis of IMN were deeply explored from the perspective of Wei qi theory. Based on the theory of “Wei qi root in kidney” and “middle jiao spleen and stomach”, combined with modern immunological cognition, Zhang Ming et al. [11] believed that “Wei qi insufficiency” was an important link in the pathogenesis of IMN. Upper jiao Xuanda, Wei qi reverse disorder, lung, spleen and kidney function damage, the ability to resist external evil, vulnerable to foreign evil attack, and “external evil, lung, spleen and kidney deficiency” is the main pathogenesis of the disease.

### 3. Traditional Chinese Medicine Treatment of IMN Methods

#### 3.1 Internal Treatment Methods

##### 3.1.1 The ancient method is applied today

“Ancient prescription for the present” is a kind of internal therapy of traditional Chinese medicine in which classical prescriptions are added or subtracted in the course of treatment and used in the treatment of diseases. Shenqi Dihuang Decoction, Zhenwu decoction and Sijunzi Decoction are the main prescriptions commonly used in the treatment of IMN. Wang Kexin [12] applied supplemented Shenqi Dihuang Decoction to the clinical treatment of IMN patients with spleen-kidney deficiency and dampness turbidity-blood stasis. The research results confirmed that supplemented Shenqi Dihuang Decoction can effectively reduce proteinuria in IMN patients, increase the level of serum albumin, effectively improve the kidney function of patients and delay the progression of the disease. At the same time, the application of added Shenqi Dihuang Decoction in the treatment of IMN patients did not appear abnormal liver and kidney function, etc. Added Shenqi Dihuang Decoction in the treatment of spleen and kidney deficiency and wet turbidity blood stasis type IMN has a high safety. Yan Junhui et al. [13] used Zhenwu Decoction and Shenzhe Decoction in the clinical treatment of IMN patients with acute kidney injury, and believed that Zhenwu Decoction has the effect of warming Yang and regulating water, and can be used for the treatment of Yang-deficiency and water-induced syndrome. Shenzhu Decoction has the effect of tonifying kidney and essence, and can be used for the syndrome of Taiyin deficiency and cold drink. On the basis of the original prescription, the addition or reduction of Shenzhu decoction has a particularly significant effect on the treatment of IMN, which can effectively regulate the immune inflammatory factors and play a significant inhibitory effect on the M-type phospholipase a2 (PLA2R) antibody of membranous nephropathy, which can reduce the kidney injury of patients and improve the clinical symptoms of patients. Guo Yinxue et al. [14] used Sijunzi Decoction combined with Zhenwu

decoction to treat IMN patients with spleen-kidney Yang deficiency syndrome. The study confirmed that in 106 patients, Chinese medicine syndrome score and 24h urinary protein quantity decreased significantly in 75 patients during 12 weeks of follow-up, and only 35 patients were judged to be ineffective after 8-12 weeks of treatment. It is believed that Sijunzi Decoction combined with Zhenwu Decoction can be used as a supplementary program of immunosuppression and hormone therapy, and it has certain effect in improving clinical symptoms of IMN. On the whole, there are some differences between the research results obtained by this scholar and those of domestic scholars, which may be caused by the difference in sample size and severity of IMN, resulting in the final curative effect of TCM treatment is not significant.

In addition to the above-mentioned ancient prescriptions, Buyang Huanwu Decoction and Shengyang Yiwei Decoction have been gradually applied to the treatment of IMN. An animal test on IMN confirmed that Buyang Huanwu Decoction and Shengyang Yiwei Decoction had obvious protective effect on the kidney of IMN rats, which may be closely related to the up-regulation of kidney protein and CD2-related protein expression of Buyang Huanwu Decoction and Shengyang Yiwei decoction [15]. Wang Dongyan et al. [16] used modified Buyang Huanwu Decoction in the clinical treatment of IMN in the study, and believed that Buyang Huanwu Decoction has the effects of invigorating qi, promoting blood circulation and clearing collateral. The use of this prescription in the treatment of IMN can effectively improve the clinical symptoms of patients, regulate the level of lipid metabolism of patients, and delay the further deterioration of kidney disease.

##### 3.1.2 Self-formulation of the test formula

With the rapid development of traditional Chinese medicine, on the basis of following the basic principle of “holistic concept, syndrome differentiation and treatment” of traditional Chinese medicine, combined with the symptom characteristics of modern IMN patients, many doctors have different opinions on the classification of IMN syndrome differentiation, but they reach an agreement on the principle of overall treatment of IMN, and all believe that the treatment of IMN should follow the principle of “tonifying kidney, invigorating spleen, benefiting qi and promoting blood circulation”. Professor Chen Yiping [17] believes that the main diseases of IMN are “wind, dampness, heat and blood stasis”, and the pathogenesis is “original deficiency and deficiency”. On the basis of clear etiology and pathogenesis, he puts forward that the treatment of IMN should follow the treatment method of “activating blood stasis, strengthening spleen and supplementing Qi, clearing heat and diuresis”, and the application of his original Chen’s kidney 9 prescription can effectively reduce IMN urinary protein. At the same time, compared with the traditional hormone therapy, Chen’s Shen9 formula has the advantages of high safety and remarkable efficacy, and can play a significant role in protecting the kidney of IMN patients during the course of medication. Duo Huiling et al. [18] took 36 cases of IMN patients with spleen deficiency and kidney stasis type as the research objects. Based on conventional Western medicine treatment, supplemented with self-prepared Jianpi Lishuitongluo formula, they found that the application of this formula could

significantly reduce the urinary protein content of IMN patients, regulate their serological indexes (serum albumin, triglycerides, cholesterol, etc.), and strengthen the protection of the kidneys of IMN patients. Effectively improve the clinical symptoms and manifestations of IMN patients and significantly improve the clinical treatment effect. Zhuang Kesheng et al. [19] used self-made Qiteng Tongluo Yin for 50 cases of IMN patients, which consisted of Radix Astragalus, Luoshi Teng, Qingfeng teng, subspatholobi, stir-fried white art with bran, white Poria, coix seed, etc. Combining it with western medicine tacrolimus can effectively relieve clinical symptoms of IMN patients and improve kidney function of patients.

### 3.2 External Treatment

Acupuncture is the most commonly used external treatment of traditional Chinese medicine, which is divided into two types: acupuncture treatment and moxibustion treatment. Acupuncture and moxibustion has the effect of warming channels and clearing collages, fuzheng and dispelling evil, and the effect of different acupoints is significantly different. In recent years, acupuncture and moxibustion has been gradually introduced into the clinical treatment of IMN and achieved certain results. In the study of Li Zheng et al [20-22], acupuncture therapy combined with western medicine was applied in the clinical treatment of patients with severe, mild and moderate membranous nephropathy. Sanyinjiao, Zusanli, Pishu, Shenshu and other points were used as the main points, and Quchi, Qihai and other points were used. The combined application of methylprednisolone cyclophosphamide, Candesartan ester tablets, methylprednisolone and tacrolimus respectively in the treatment of patients with severe, mild and moderate membranous nephropathy, the study results showed that acupuncture combined with Western medicine in the treatment of patients with severe, mild and moderate membranous nephropathy has a significant effect, which can effectively reduce the physiological indicators of patients and improve the clinical therapeutic effect. However, the clinical study of acupuncture in the treatment of IMN is rare, and the specific effect of acupuncture in the treatment of IMN has not been confirmed clinically.

Moxibustion, as one of the typical external treatment methods of traditional Chinese medicine, has the effect of tonifying blood and qi, warming channels and collaterals, and can be used to treat IMN caused by “deficiency and deficiency”. Mao Jingyu et al. [23] selected 60 patients with spleen-kidney deficiency complicated by blood stasis syndrome and low-to-medium risk IMN as research subjects in their study, investigating the effects of moxibustion on renal function and hypercoagulable state in these patients. Shenshu, Guanyuan, Qihai, Pishu, Zusanli and Sanyinjiao were used as the main points, and moxibustion treatment was carried out with moxibustion, once a day, continuous treatment for 5d and 2d rest, continuous treatment for 6 months. Comparing moxibustion therapy with traditional Western medicine, it was found that moxibustion combined with traditional Western medicine can effectively improve the clinical symptoms of IMN patients and get rid of hypercoagulability. Effectively improve the patient’s kidney microcirculation and then play a protective role in its renal function, with significant curative effect and high safety advantages. At the

same time, Guo Hongying et al. [24] used Huangqi Zosh Bushen recipe combined with moxibustion in the clinical treatment of 30 patients with IMN. Moxibustion treatment was performed on points such as Sanyin Jiao, Zusanli, Pishu and Shenshu for a total of 6 months. The research results confirmed that Huangqi Zosh bushen recipe combined with moxibustion can effectively reduce the clinical symptoms of patients and reduce the damage of kidney tissue. Improve blood lipids and other related indicators. In summary, the studies on external treatment of IMN by traditional Chinese medicine are relatively rare and the intervention time of most studies is relatively short. The specific efficacy and safety of external treatment of IMN still need to be further explored.

### 3.3 Other Therapies

With the continuous development of clinical studies, some researchers have found that the clinical effect of treating IMN by traditional Chinese medicine alone is not significant. Therefore, the combination of traditional Chinese and Western medicine in the treatment of IMN has gradually become the focus of clinical research. Huang Xiayun et al. [25] used Huangmallow capsule combined with methylprednone in the clinical treatment of elderly IMN patients, and the research results confirmed that this treatment can effectively improve the renal function and lipid related indexes of elderly IMN patients. At the same time, the combination of drug use did not increase the probability of adverse reactions, which confirmed that the clinical efficacy of combined drug use in the treatment of IMN was particularly significant and high safety. Deng Tao et al. [26] applied Zhengqing Fengtongning combined with prednisone tablets in the clinical treatment of IMN, and found that the application of combined treatment could significantly reduce the TCM syndrome score of IMN patients, improve the serum protein level of patients, reduce the urine protein content, and improve triglyceride and other lipid indexes. In addition, most studies have confirmed that the combination of traditional Chinese and western medicine in the treatment of IMN has the advantages of high safety and small toxic side effects [27-29].

In addition, dietary therapy is one of the ways to treat diseases in traditional Chinese medicine. IMN is a chronic disease. Good living habits and eating habits are important ways to delay the progression of IMN. Therefore, some clinical scholars believe that dietary therapy can be used as an adjunct treatment for IMN. On the basis of previous studies, Nie Lifang [30] established the IMN dietary experience formula Astragalus carp soup, which is composed of carp or crucian carp plus raw Astragalus, chixiao bean and amomum kernel. This diet method is suitable for patients with Yin deficiency of the spleen and stomach and IMN stoppage in the water dampness.

## 4. Conclusion

To sum up, traditional Chinese medicine believes that the pathogenesis of IMN lies in “deficiency of origin and deficiency of substance”, and “tonifying kidney, invigorating spleen, invigorating qi and promoting blood” is the fundamental follow of TCM treatment of IMN. With the continuous deepening of clinical studies, although TCM treatment of IMN has been developed to a certain extent, there

are still shortcomings, such as: clinical studies mostly use TCM treatment combined with immunosuppressive therapy, and the sample size is small and single-center studies, lacking multi-center studies. At the sametime, there are relatively more studies on the internal therapy of traditional Chinese medicine, and relatively few studies on the external therapy. Therefore, the sample size should be continuously expanded in the follow-up studies on the treatment of IMN with traditional Chinese medicine, focusing on the efficacy of acupuncture, moxibustion and other external therapies for IMN, and enriching the clinical treatment means of IMN.

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