

Progress in the treatment of gouty nephropathy with Chinese and Western medicine

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Abstract: With the continuous development of science and technology, the improvement of public quality of life and poor dietary habits, the incidence of hyperuricemia is increasing year by year, and the incidence of complications caused by it, such as gouty arthritis and gouty nephropathy, is also gradually increasing, and severe cases may even develop into end-stage renal disease, which seriously reduces people's quality of life and survival rate. At present, the purpose of reducing uric acid and protecting kidney is mainly achieved by combining traditional Chinese and western medicine. The Western medicine treatment of gouty nephropathy mainly adopts inhibition of uric acid synthesis, promotion of uric acid excretion or acceleration of uric acid decomposition to achieve the purpose of reducing uric acid, while taking into account the treatment of other complications such as kidney protection, blood pressure, hypoglycemia and lipid regulation. Through the combination of internal and external treatment such as syndrome differentiation, acupuncture or Chinese medicine application, Chinese medicine has the purpose of lowering uric acid to protect the kidney and delay the progression of the disease. This paper reviews the treatment of gouty nephropathy by Chinese and western medicine through reading domestic and foreign literatures, and provides reference materials for clinical treatment.

1. Introduction

Gouty nephropathy (GN), also known as uric acid nephropathy (UAN), refers to reduced excretion and/or excessive production of uric acid (UA) in the body, leading to hyperuricemia (HUA), and then kidney damage caused by the accumulation of urate crystals in the kidney [1]. With the rapid development of economy and the improvement of residents' living standards, the prevalence rate of HUA is increasing year by year and has gradually become the second largest metabolic disease after diabetes [2]. HUA is considered as one of the independent risk factors for the occurrence and further deterioration of chronic kidney disease (CKD) [3]. In this paper, the research progress of Chinese and Western medicine on GN in recent years is summarized as follows.

2. Advances in Western medicine research

The occurrence of gouty nephropathy is related to HUA and urate crystal deposition in the kidney. UA is the end product of human exogenous purine metabolism, which is mainly produced in the liver, intestine and vascular endothelium, of which about two-thirds are excreted by the kidney, and about one-third is excreted through the intestine[4]. If the production and/or excretion function is impaired, the UA level in the body is abnormal, resulting in the formation of HUA[5]. A large amount of urate crystals deposited in the kidney can damage the renal tubule interstitium and even cause glomerular fibrosis, thus affecting the excretory function of the kidney, namely the formation of GN[6].

2.1 Pathogenesis of Western Medicine

At present, the pathogenesis of GN is mainly as follows:

- Promoting inflammatory response. For example, urate crystallization can further promote the release of inflammatory cytokines by stimulating and activating the NOD-like receptor protein 3 (NLRP3) inflammasome[7].

- Oxidative stress reaction. Reactive oxygen species (ROS) is one of the by-products of UA formation. Excessive ROS can cause oxidative stress and promote inflammation. Oxidative stress can affect the function of mitochondria in renal tubular epithelial cells, thus inducing apoptosis of renal tubular epithelial cells[8].

- Activation of renin-angiotensin aldosterone system (RAAS). One of the driving factors for the progression of CKD is inflammation, which interacts with oxidative stress, and RAAS can promote inflammation and oxidative stress[8].

- Endothelial dysfunction. Studies have shown that UA changes the endothelial structure by reducing the production of nitric oxide (NO), activating RAAS, causing oxidative stress, etc., affecting endothelial function, and thus affecting kidney function[9].

- Induced renal fibrosis. UA can induce renal fibrosis through cell transdifferentiation, activation of RAAS, promotion of proliferation of renal vascular smooth muscle cells, oxidative stress and autophagy[9].

At present, it is known that the occurrence of UN is related to various signaling pathways [10]. Sui Xiaolu et al.[11] suggested that GN is closely related to signaling pathways such as phosphoinositol 3 kinase, protein kinase B, and nuclear transcription factor- κ . Zhao Huiwen et al.[12] found through experimental studies that the occurrence of UN inflammation may be related to interleukin-1 (IL-1) β and interleukin-1 receptor-associated kinase 4 (IRAK-4). This provides a new idea for the clinical treatment of UN.

2.2 Western Medicine Treatment

The disease usually starts with tubular interstitial injury, and the main clinical manifestations are often tubular concentration dysfunction such as polyuria, nocturia, hypogravity urine or even microscopic hematuria[13]. In the middle and late stages of development, glomerulus may be involved, often manifested as persistent proteinuria or even hematuria, renal function abnormalities such as increased creatinine (Scr), uric acid, urea nitrogen (BUN), and decreased glomerular filtration rate, and eventually chronic renal failure[14]. During the treatment of GN, the protection of renal function should be carried out throughout, and all treatment should be based on the premise of not damaging the kidney[15]. The treatment should follow the following three principles: basic treatment, etiological treatment and alternative treatment.

2.2.1 Basic treatment

Diet control (low purine, low salt, low fat, low protamine diet, avoid animal viscera, animal viscera and spicy and irritating food, etc.) Drink plenty of water, it is recommended to drink more than 2000ml/d.) Quit smoking and drinking. Alkalized urine: When urine pH is controlled between 6.2 and 6.9 and urine pH is <6.0, it is necessary to alkalize urine to prevent the formation of stones, and citric acid preparation or sodium bicarbonate are often used clinically[16]. Patients with acute gout should be treated with non-steroidal anti-inflammatory drugs (NSAIDs) or hormone therapy. Studies suggest that corticosteroids should be the first choice for most patients with CKD and gout attacks[17], and NSAIDs should be prohibited for patients with end-stage kidney disease (ESRD)[18]. Colchicine is contraindicated in patients with acute gout attack combined with kidney injury[19]. Other symptomatic treatment: kidney care, correct electrolyte disorders, acid-base imbalance. Control blood pressure, blood sugar, blood lipids, anti-infection, etc.

2.2.2 Etiological treatment

Means to control UA within the normal range. The target value of treatment UA was controlled within 360 μ mol/L. Combined with diabetes, hypertension, cardiovascular and cerebrovascular diseases, uric acid calculi, CKD2 stage and above, UA should be controlled at 300 μ mol/L[20].

Studies have shown that hypouricemia is one of the factors of renal function impairment in healthy people, and it is recommended to control UA not less than 180 μ mol/L[21]. There are two classes of drugs commonly used in clinical practice to reduce uric acid: inhibition of uric acid synthesis: representative drugs allopurinol and febuxosita, which reduce UA by inhibiting xanthine oxidase activity; Promotion of uric acid excretion: representative drug benbromarone, which reduces UA by inhibiting renal tubule reabsorption of urate[18]. Allopurinol is contraindicated in patients with stage 5 CKD and febuxoat at conventional dose in patients with mild to moderate kidney injury [22].

2.2.3 Renal replacement therapy

For patients with chronic kidney failure, choose the appropriate dialysis treatment (peritoneal dialysis or hemodialysis) or kidney transplantation.

3. Progress in TCM research

There is no disease name of GN in ancient Chinese medicine books[23], which can be divided into the following categories according to its clinical manifestations and affected parts: joint damage can mainly be classified as "bi syndrome" and "gout"; Kidney involvement can be classified as "longbi", "edema", "hematuria", "kidney failure disease" and so on.

3.1 Etiology and pathogenesis of TCM

Traditional Chinese medicine believes that the basic pathogenesis of GN is deficiency with deficiency. The acute phase is mainly characterized by standard deficiency, and the remission phase is mainly characterized by primary deficiency. The chronic disease affects collaterals and joints or even kidneys, resulting in renal failure [24]. Contemporary doctors believe that the pathogenesis of GN is based on deficiency of healthy qi, deficiency of both spleen and kidney, or deficiency of both liver, spleen and kidney, and the main pathological factor is phlegm turbidity and dampness stasis[20]. Professor Zhang Xikui believed that[25]GN phlegm- dampness -heat toxicity was caused by internal depression, qi stagnation and blood stasis, which was caused by the interaction of

multiple factors. Professor Chen Dai believed that the etiology and pathogenesis of [26]GN were complex and varied. Water, dampness, phlegm, stasis and poison were pathogenic factors and pathological products, and a vicious cycle eventually caused kidney involvement. Professor PI Zhiheng believed that [27] gouty nephropathy was mainly caused by excessive eating of fat and sweet taste, dampness, blood stasis and internal withdrawal of poison, which resulted in spleen and kidney damage and spleen and kidney deficiency.

3.2 TCM Treatment

3.2.1 TCM internal treatment

Professor Wang Zimin [28] GN is usually treated by stages in clinical treatment. In the acute phase, wind-cold and dampness bi or rheumatic heat bi is the main treatment, and the treatment should be dispelling wind and dampness, warming Yang and dispelling cold, or clearing heat and dampness, dispelling wind and clearing luo. Chronic convalescence is mainly due to spleen-kidney qi deficiency and dampness and turbidness in spleen-kidney deficiency or Qi-yin deficiency and blood stasis. The treatment should strengthen spleen and kidney, remove dampness and water, or warm Yang and spleen, remove dampness and turbidness, with activating blood stasis, or activating qi and Yin and activating blood circulation. Professor Li Peixu [29] divided the TCM differentiation and treatment of GN into acute attack stage and chronic progressive stage. According to the etiology and pathogenesis of the different prescription drugs are very different. Acute stage to treat symptoms, should be qingli dampness-heat, xuanbi Tongluo. Chronic period of treatment of its main, it is appropriate to benefit the kidney and spleen, to treat symptoms of appropriate dampness Tongfu, detoxification and stasis. Professor Zhong Ying [30] In the clinical treatment of GN, the basic principles are often both attack and tonic treatment and the same treatment of specimens. Attack, mainly detoxification and turbid drainage, pay attention to attack evil does not hurt positive. Wei Jinhua et al. [31] randomly divided 74 UN patients into the control group and the treatment group with 37 cases in each group. The control group was given oral allopurinol tablets under basic treatment, and the treatment group was given oral cicornithoate capsules on the basis of the control group.

3.2.2 TCM external treatment

Studies have shown [32] that during the acute attack of gout, phlegm stasis, damp-heat, turbid-toxin blockage of meridian channels are the main methods, and Chinese medicine application based on the principles of diuresis and turbidity-releasing, clearing heat and detoxification, removing blood stasis and dredging collaterals has great advantages in alleviating the pain of gout. Clinical studies have shown [33] that external treatment combined with Western medicine has a more significant effect than western medicine alone in treating acute GA. TCM external treatment methods such as acupuncture, external application of Chinese medicine, Chinese medicine fumigation, enema, etc., are effective in treating acute GA and can often quickly relieve clinical symptoms [34]. External application of supplemented Sihuang paste [35] can rapidly reduce clinical symptoms such as redness, swelling, heat and pain in acute GA patients, improve curative effect, and is inexpensive, simple to operate, and has no obvious adverse reactions. Acupuncture can reduce the level of inflammatory factors and improve the symptoms of redness, swelling and heat pain, and its curative effect on GA is clear [36]. Studies have shown [37] that acupuncture treatment can significantly reduce the UA level of patients and alleviate the damage to liver and kidney. Liu Dunyu et al. [38] randomly divided 72 patients with chronic GA into a control group (36 cases) and an observation group (36 cases). The control group was treated with western medicine and the

observation group was treated with traditional Chinese moxibustion. The results showed that the total effective rate of observation group was 94.44%, which was significantly higher than that of control group, suggesting that moxibustion can improve the effective rate of chronic GA patients. Studies have shown [39] that TCM enema can absorb drugs directly through the abundant blood vessels in the rectum, with fast absorption speed and no liver damage, and exert its function of clearing fu-organs and expelling turbidousness and detoxification.

4. Experimental Research

The results showed that [40] *Psyllium frustum* aqueous decoction had anti-GN effect by decreasing the expression of NLRP3 inflammasome signaling pathway protein in rat kidney tissue. Bai Li et al. [41] randomly divided 84 mice with GN model into 7 groups, including control group, model group, allopurinol group, Tongfengshu group and three different doses of peony total flavonoids group. The results showed that the content of UA and Cr in peony total flavonoids group decreased, only the degree of decrease was different, that is, peony total flavonoids can play a role in protecting kidney by reducing UA and Scr. Jin Wenmin et al. [42] confirmed through experiments on GN model rats that Yougui Yin can play a role in protecting kidney by reducing UA, BUN, Scr and urinary protein quantitative (24hU-TP) levels of rats. Li Yuxuan et al. [43] confirmed through experimental studies that *atletia Baihu* Decoction has the same mechanism of action as allopurinol and feburestat, which can inhibit the production of UA by inhibiting the activity of xanthine oxidase, and at the same time inhibit the expression of interleukin1 β and TGF- β 1 in kidney tissue, playing a role in protecting the kidney. The research results showed [44] that baicalin and baicalein could both reduce UA levels in mice with UN model in vivo and in vitro, and play a role in protecting kidney through multi-target and multi-pathway, with no significant difference in results.

5. Conclusion

As a complication of HUA or GA, the key to the prevention and treatment of GN is to effectively control UA level. It is recommended that patients develop scientific eating habits, limit salt and control sugar, low purine diet, quit smoking and alcohol, and drink a moderate amount of water. It is recommended that patients regularly check the relevant indicators of target organ damage such as kidney function to prevent complications, so as to achieve early detection and early treatment. Western medicine has not fully clarified the pathogenesis of GA, but most scholars believe that it is related to the kidney damage caused by the accumulation of urate crystals in renal tubule interstitium. Symptomatic treatment is the main treatment for GA. Current studies suggest that HUA needs to take uric-lowering drugs for a long time to achieve the goal of stable control of uric acid, but these drugs may cause adverse reactions to varying degrees, such as inducing the attack of gout. After drug withdrawal, repeated illness and elevated uric acid are easy to cause poor compliance of patients, so it is urgent to find an effective treatment plan for gouty nephropathy. Through holistic thinking and dialectical treatment, traditional Chinese medicine can comprehensively regulate the internal environment of the patient's body, stably control uric acid at the standard level, improve renal fibrosis, protect renal function, and delay the progression of the disease. The treatment of GN by traditional Chinese and western medicine has its own advantages and disadvantages. How to find the joint point, control the disease while preventing related complications, delay the progression of kidney disease, is an important direction of medical research and development in the future.

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