

Research Progress in the Treatment of Early Diabetes Nephropathy with Traditional Chinese Medicine

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Abstract: DN (diabetes mellitus) is a common chronic disease that harms human health, and it is also one of the common complications of DM (Diabetes mellitus) in clinic. DN is a serious hazard to human health, and it is one of the main causes of death of DM patients. At present, there is no specific curative method for its treatment. The intervention of EDN (Early diabetic nephropathy) is particularly important for patients. If timely and effective treatment is given in the early stage of DN, renal damage can be reversed and the progress of the disease can be delayed. In recent years, Chinese medicine has made some achievements in the prevention and treatment of EDN, and at the same time, it has accumulated rich experience in the research of treating EDN with Chinese medicine. Various studies have shown that Chinese medicine has certain advantages in preventing and treating the occurrence and development of DN and delaying the deterioration of renal function, with positive curative effect and no obvious toxic and side effects. Based on this, this article mainly discusses and analyzes the research progress of traditional Chinese medicine (TCM) in treating EDN, and reveals that TCM is of great significance in improving the clinical symptoms of DN and delaying the progress of the disease.

1. Introduction

DM is one of the most important non-communicable diseases that threaten the global human health at present. Many kinds of chronic complications caused by DM in the middle and late stages are important reasons for disability and death of patients[1]. DN is mainly caused by diabetic microangiopathy and is one of the serious complications of DM[2]. It can eventually lead to end-stage renal failure and even death in DM patients. The basic pathological features of DN are glomerular capillary basement membrane thickening, mesangial matrix hyperplasia and glomerulosclerosis; The main clinical manifestations are proteinuria, hypertension, edema and varying degrees of renal function damage[3]. At present, DN has become the main cause of ESRD. It is reported that DN incidence rate in type 1 DM is 40%~50%, and DN incidence rate in type 2 DM is 20%~30%[4]. At present, the quantity of DM patients in China is increasing, and the quantity of DM patients worldwide is also increasing. The prevalence of DN is increasing year by year, and the situation cannot be ignored. At present, the pathogenesis of DN has not been clarified,

and there is a lack of specific drugs and therapies in clinical practice[5]. Modern medicine still lacks specific and effective treatment methods.

According to clinical data statistics, about 30%~50% of DM patients will have DN, which seriously endangers the physical and mental health of DM patients. DN is characterized by massive proteinuria, hypertension, edema and progressive renal function loss. In China, DN is the second cause of ESRD, second only to glomerulonephritis[6]. It is generally believed that the natural course of DN is gradual, starting from proteinuria, and then developing into ESRD through two stages of microalbuminuria and dominant proteinuria. Therefore, the intervention treatment of EDN may reverse the reversible renal damage and delay the progress of the disease[7]. TCM has a long history of treating this disease, and with the research of modern doctors, it has achieved satisfactory results in preventing the occurrence and development of DN. For this disease, early treatment and intervention are of great significance[8]. In recent years, TCM has accumulated rich experience in treating DN, especially in the treatment of DN, which shows the unique advantages of TCM. It can significantly improve the symptoms of patients, reduce proteinuria, improve renal function and delay the progression of DN[9]. A large quantity of studies have shown that on the basis of diet, exercise and hypoglycemic drugs, the addition of TCM has a good effect[10]. To sum up, this article summarizes all aspects of DN, mainly studies and discusses the research progress of TCM in treating EDN, and reveals that TCM is of great significance in improving clinical symptoms of DN and delaying disease progression.

2. Etiology and Pathogenesis

Most doctors believe that DN belongs to the syndrome of deficiency and excess, which is closely related to the causes of insufficient endowment, emotional failure, deficiency of yin in the body, and excessive exertion. Throughout the clinical research and observation of DN in modern Chinese medicine, various doctors have their own views on the pathogenesis of DN. “Lingshu · Five Changes” said: “Those who are weak in the five internal organs are good at disease and disease.” Eating inappropriately for a long time, eating fat and sweet, mellow wine and thick taste, spicy and dry, damaging the spleen and stomach, resulting in the failure of the spleen and stomach to function, accumulating heat inside, transforming dryness and hurting the body, eliminating grain and liquid consumption, and causing thirst. In addition to eating inappropriately, emotional disorder is also a major cause. Long-term excessive mental stimulation leads to depression turning into fire, burning in the fire, burning the lung and stomach yin and causing thirst. Over time, fluid and qi are exhausted, and qi deficiency and yang develop into EDN. Xiong Wei investigated the distribution characteristics of TCM syndromes in early patients, and showed that the syndrome types with high incidence of EDN stage were Qi and Yin deficiency syndrome (53.18%), liver and kidney yin deficiency syndrome (46.12%); Blood stasis syndrome has the highest frequency (60.0%)[11]. Song Qiangqiang et al. believed that “internal toxicity” was the initiating factor for the conversion of DM to DN, and proposed that there were three main ways of its generation: ① various wastes generated by the body in the stage of metabolism; ② The substances needed for normal physiological activities of the human body are accumulated due to metabolic disorders exceeding consumption; ③ Physiological substances become pathogenic diseases due to changing their location of existence, and the pathogenic diseases become toxic when they are depressed for a long time[12]. Liao Xin believes that DN is caused by deficiency of both qi and yin, and blood stasis and dampness are important factors for its occurrence and development. Especially in EDN, the deficiency of both qi and yin is the basis, and the standard is mostly dampness and blood stasis, which are intertwined and lingering, eventually leading to deficiency of both qi and blood, yin and yang, resulting in a variety of changes[13].

To sum up, TCM believes that the etiology of DN is mostly related to insufficient congenital endowment, improper diet, excessive labor and desire, and emotional disorders. The most basic pathogenesis of DN is the deficiency of the root and the excess of the root. Dampness, poison and blood stasis run through the whole stage of the disease. Its occurrence and development is a dynamic process, and its formation is not the result of a single visceral lesion, but the result of prolonged illness and multiple visceral involvement, especially the spleen and kidney as the key, and finally forms the syndrome of deficiency and excess, and the syndrome of deficiency and excess is mixed.

3. Treatment of EDN with TCM

3.1 Treatment Based on Syndrome Differentiation

DN has a long course of disease and is one of the chronic diseases that are difficult to treat in clinic. The disease is complicated due to the conflict between good and evil. We should focus on the etiology and pathogenesis, grasp the differentiation of symptoms and signs, treat both symptoms and signs, and use rational drugs to delay the development of the disease as much as possible and stabilize the disease. Chen Luyan et al. divided DN into qi and yin deficiency type, kidney deficiency and blood stasis type, spleen and kidney deficiency type, and qi deficiency and blood stasis type, and divided them into control group and treatment group. The results show that Chinese medicine can not only significantly improve the clinical symptoms of EDN patients, but also reduce the urinary albumin excretion rate (UAER) of EDN patients, improve glomerular hyperfiltration, protect renal function, and reduce the level of serum hypersensitive C-reactive protein[14]. Lin Lan et al. divided EDN into: ① yin deficiency and heat exuberance through clinical research and referring to the Diagnostic and Treatment Standard of Integrated Traditional Chinese and Western Medicine for DM. ② Deficiency of both qi and yin. ③ Deficiency of yin and yang. ④ Concurrent blood stasis syndrome[15]. Huang Yanqin and others observed that the Tangluotong decoction, which is composed of the method of tonifying the kidney and activating blood circulation and dredging collaterals, was added or decreased according to the symptoms, and 68 cases of EDN were treated. Results The total effective rate was 89.47% in the treatment group and 60% in the control group; Compared with the control group, it has a better effect in reducing urinary micro-protein, plasma endothelin and nitric oxide[16]. DN is one of the common chronic diseases in clinic, and its condition is complex. At the early stage of the disease, it is mostly based on the deficiency of both qi and yin, and at the same time, it is mixed with the syndrome of blood stasis, phlegm, dampness and turbidity, among which blood stasis runs through the course of the disease. Therefore, we should not only treat yin deficiency and dryness and heat, but also pay attention to the application of the therapy of activating blood circulation and removing blood stasis.

3.2 Single Chinese Medicine and Extract

Astragalus has the effects of tonifying qi, strengthening spleen, diuresis and detumescence. Clinical studies have shown that astragalus can improve nitric oxide (NO), urinary microalbumin excretion rate (UAER), calcitonin gene-related peptide (CGRP) and endothelin-1 (ET-1) in patients with EDN, reduce urinary protein and delay the occurrence and development of EDN. Li Chen et al. selected 105 patients with EDN and randomly divided them into treatment group (53 cases) and control group (52 cases). Both groups were treated with hypoglycemic drugs, and the treatment group was treated with Qiming granules in addition to the treatment based on DM. After 3 months of medication, it was found that HbA1c, TC, LDL-C, ACR, CysC, FBG β The indexes of 2-MG and UAER were significantly improved compared with those before treatment, but there was no

significant change in the control group. This study confirmed that Qiming Granule can significantly improve renal function, reduce renal injury, reduce blood glucose and blood lipids, and can safely and effectively delay the development of DN[17]. Wu Yan et al. randomly divided 70 cases of EDN into two groups. The treatment group took Tongmai Jiangzhi Pill orally on the basis of routine treatment, and the urine microalbumin decreased after 8 weeks of treatment[18]. Wang Guanghao and others used 30 ml of astragalus membranaceus to add it to normal saline for intravenous injection and insulin treatment. After treatment, UAER, FBG, TC and TG of 40 patients decreased significantly ($P<0.05$). Experimental research shows that astragalus can improve the plasma endothelin level in patients with EDN, increase the synthesis of nitric oxide in the kidney, and have a protective effect on renal vascular endothelial cells[19]. Xiao Xueyun first treated 40 cases of EDN with conventional western medicine, and then added Niaoduqing granules, which significantly decreased the urine micro-protein. Niaoduqing granules can effectively delay the stage of early renal damage in DN.

3.3 TCM Injection and Acupuncture and Moxibustion Treatment

At present, the commonly used injections for clinical treatment of this disease include: astragalus injection, Shenkang injection, Shuxuening injection, salvia miltiorrhiza injection, ginkgo biloba injection, etc. Hao Yujie et al. treated 53 patients with this disease with Shenkang injection and set up a control group. Results The treatment group was superior to the control group in reducing UAER, ET-1, blood cholesterol and improving renal function, blood lipids and plasma viscosity ($P<0.05$)[20]. Li Xingbo et al. treated DN with self-designed invigorating spleen, supplementing qi and activating blood circulation formula combined with warm acupuncture. The results showed that the quantitative level of urinary protein and the ratio of microalbumin/creatinine in urine of the patients after treatment had obvious advantages. Zhang Zhilong et al. divided 144 patients with DN into observation group and control group according to random number table method, with 72 patients in each group. On the basis of routine treatment, the observation group was treated with acupuncture for regulating the spleen and stomach; The control group took Shenshu, Taixi, Sanyinjiao, Yanglingquan and other points according to the teaching material of acupuncture and moxibustion. The two groups were treated twice a day, with 6 days as a course of treatment. After 1 day of rest, the second course of treatment was continued for a total of 6 weeks[21].

3.4 Other Therapies

In addition to the above treatment methods, TCM also has TCM enema, ear point sticking and pressing and other methods to treat EDN, which has also achieved good clinical results. Zhang Zhilong et al. formulated corresponding acupuncture prescriptions based on the principle of regulating spleen and kidney, and conducted clinical research on EDN patients. On the basis of routine treatment of DM, take Hegu, Xuehai, Zusanli and other points for acupuncture treatment. After treatment, the patient's UAER decreased significantly compared with that before treatment, suggesting that acupuncture combined with drugs has a better clinical effect on EDN[22]. Zhou Yi and others found that Sanshen Shenyu Decoction combined with routine western medicine treatment of DN can improve renal microcirculation, reduce renal hyperperfusion, improve urinary protein filtration and protect renal function. Li Wei found that the use of Juanbai decoction rectal drip has a good effect on the treatment of DN. After treatment, it was found that the clinical symptoms of patients in the treatment group were significantly improved, and urinary microalbumin, FPG and 2hPG were significantly decreased. The total effective rate of the treatment group (92.7%) was better than that of the control group (73.1%)[23]. Zhao Chunyan and others randomly divided 160 patients with DN into control group and TCM group, with 80 patients in each group. The

control group was treated with conventional western medicine, subcutaneous injection of insulin or oral hypoglycemic drugs were used to control blood glucose indicators, and blood pressure and blood lipid lowering drugs were taken at the same time. Chen Zhe et al. used oral perindopril plus TCM decoction Huoxue Jiangtang Decoction to observe EDN patients with syndrome differentiation of qi and yin deficiency combined with blood stasis. Blood Scr and urine after treatment β 2-MG, UAER, GDF-15 and TCM syndrome scores were significantly lower than before treatment, and the serum GDF-15 of patients was significantly lower. The results suggest that Huoxue Jiangtang Decoction can significantly reduce the level of serum GDF-15, and its mechanism is related to anti-inflammatory and antioxidant effects.

4. Conclusions

With the continuous deepening of clinical research on EDN, TCM has achieved satisfactory results in treating EDN. The treatment of TCM and the early stage of EDN have made great progress and development, and the treatment method has formed a situation of blooming flowers and competing flowers. The treatment of DN with TCM has achieved good curative effect, which can not only control the development of the disease, but also improve the symptoms in the advanced stage. It can be treated flexibly through syndrome differentiation and analysis, and has the characteristics of prominent curative effect of symptoms, less adverse reactions, and precise effect of prevention and control of complications. The unique advantages of TCM in the treatment of DN fully show the idea of treating disease before disease in TCM, and show a good application prospect. In this article, the research progress of TCM in the treatment of EDN is discussed, and it is expected that there will be more large-scale, multi-center randomized controlled trials for TCM in the treatment of EDN to verify the reliability of its efficacy. In addition, in the future research, we should use evidence-based medicine under the guidance of the theory of TCM, establish a unified basic syndrome type and recognized clinical efficacy evaluation standard, and carry out in-depth research on the mechanism of the treatment of EDN system with TCM, as well as multidisciplinary and multi-channel comprehensive research; In combination with modern pharmacology, we have developed and developed precise and effective new drugs of TCM to systematize and standardize the treatment of TCM in EDN.

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