

Research Progress of Chinese Medicine External Treatment in Diabetic Nephropathy

Wen Yan, Xiaohui Li*

Shaanxi University of Chinese Medicine, Xianyang, 712000, China
Wenzi202303@163.com
*Corresponding author

Abstract: With the deepening of clinical research related to Chinese medicine, it is found that external treatment of Chinese medicine can improve the clinical symptoms of DN patients, improve the quality of life, delay the progression of diabetic nephropathy, and to some extent alleviate the adverse effects of drugs on the body, as the so-called "the theory of external treatment is the theory of internal treatment; the medicine of external treatment is the medicine of internal treatment.....", the external treatment method of Chinese medicine is also the same as the principle of internal medicine of Chinese medicine, according to the patient's condition, the diagnosis and treatment, the recent research progress of the external treatment method of Chinese medicine for DN is reviewed.

Keywords: Chinese medicine external treatment; Diabetic nephropathy

1. Introduction

Diabetic nephropathy (DN) is a chronic kidney disease caused by diabetes mellitus (DM), which is the most common microvascular lesion in DM. The main clinical manifestation is persistent proteinuria and progressive decline in renal function^[1]. Some data show that the latest prevalence of DM in Chinese adults is about 12.4%, which is significantly higher than the global rate (8.3% in 2019)^[2]. With the subsequent increase in the prevalence of DKD year by year, it has become the leading cause of chronic kidney disease in China^[3]. Meanwhile, DN is the leading cause of end-stage renal disease (ESRD), and the burden of medical treatment and death caused by DN continues to increase, seriously endangering people's health. The treatment of DN in modern medicine mainly focuses on improving poor lifestyle and controlling high-risk factors such as blood glucose, blood pressure and lipids to protect the kidney and alleviate the progression of the disease^[4]. With the continuous clinical research related to TCM, it was found that external treatment of TCM can improve clinical symptoms, improve quality of life, delay the progression of DN in DN patients, and alleviate the adverse effects of drugs on the organism to a certain extent^[5]. As the saying goes, "The principle of external treatment is the principle of internal treatment; the medicine of external treatment is the medicine of internal treatment.....", the principle of external treatment of TCM is also the same as the principle of internal medicine of TCM, which needs to be administered according to the patient's condition. The recent research progress in the treatment of DN by external Chinese medicine is reviewed.

2. DN etiology and pathogenesis

In Chinese medicine, there is no name for diabetic nephropathy. Most of the clinical manifestations of the disease are classified as "edema", "urinary turbidity", "guangs", and "deficiency labor" related to the disease of thirst, "deficiency labor" and other categories^[6]. This disease is caused by deficient endowment of the body. The main factors of this disease include deficiency of endowment, dietary disorders, invasion of the six sexes, and emotional and mental disorders, as well as "sugar toxicity" and "lipid toxicity". Most modern medical practitioners believe that this disease is caused by the extension of the thirst disease, and the pathogenesis belongs to the original deficiency and the actual symptoms. In the early stages of DN, continuous or intermittent microproteinuria occurs, mostly due to dryness, heat and deficiency of essence, and deficiency of qi and yin; in the later stages, the disease develops further, with edema, massive proteinuria and continuous progression of renal function. Modern medicine believes that the pathogenesis of DN is not yet clear and is very complex, mainly due to disorders of glucolipid metabolism, abnormal renal hemodynamics, oxidative stress, inflammatory

mechanisms, and genetic background [7].

3. Traditional Chinese Medicine External Treatment

3.1 Acupuncture therapy

Acupuncture is based on the action of meridian acupoints on the human body, to achieve the purpose of dredging the meridians, harmonizing qi and blood, yin and yang to prevent and cure diseases, and in recent years, the combination of acupuncture and medicine is the main way to treat diabetic nephropathy. Liu Liang Liu Liang [8] et al. found that "regulating the spleen and stomach acupuncture method" (bilateral Quchi, Feet Sanli, Diji, Zhongbei, Yinlingquan, Hegu, Sanyinjiao, Baiwuzhao, Fenglong, and Taichong) could increase the levels of PCX, CD2AP, nephrin protein, and gene expression in renal foot cells, thus decreasing desmin protein activity, in order to improve DN foot cell injury in rats, reduce glomerular basement membrane thickening, decrease urinary protein content, improve blood lipids and renal function, and delay the progression of DN. Ye Zhenghua [9] et al. treated patients with early DN evidence of qi and blood deficiency by combining traditional Chinese medicine with acupuncture, selecting acupoints such as Liver Yu, Guan Yuan, Foot San Li, Spleen Yu, Stomach Yu, Sanyinjiao, and Tai Xi, and found that the total efficiency of the treatment group was significantly higher than that of the control group, which significantly improved the patients' good renal function and improved the quality of life. Zhang Huijie [10] et al. used acupuncture combined with zhi kidney hypoglycemic formula to treat patients with DN, which could significantly alleviate patients' clinical symptoms, reduce erythrocyte aggregation index, whole blood viscosity, and vascular endothelial cell damage factor, and further improve patients' hypercoagulable state, thus preventing further development of DN, compared with the use of drugs alone. On the basis of conventional treatment in Western medicine, Rui-Ping Liu [11] et al. treated DN patients with yin and yang deficiency by acupuncture combined with Jisheng Kidney Qi Pill, and found that it could significantly improve patients' clinical symptoms such as glucose metabolism and urinary protein excretion rate, reduce the level of inflammatory factors, and protect renal function.

3.2 Acupoint injection therapy

Acupuncture point injection therapy is based on the basic theory of Chinese medicine, combined with the doctrine of meridians to inject drugs through acupuncture points for the purpose of treating diseases. Ding Yi [12] Selected double feet three li and kidney acupoints, through the Chinese medicine acupoint injection combined with warming spleen and tonifying kidney soup plus reduction for the treatment of DN with internal blood stasis, the results found that the total efficiency of treatment was significantly higher than the control group, and the clinical efficacy was significant, which could significantly reduce the blood glucose level and improve the kidney function of patients. In terms of basic treatment, Ji Zhirong [13] The use of Huangqi injection for acupoint injection at the foot Sanli and kidney acupoints, combined with the internal administration of Chinese medicine for the treatment of early DN patients, was found to effectively reduce urinary albumin, improve DN symptoms, and protect renal function. Zhao Cheng [14] Treating DN III-IV patients with DN by acupoint injection combined with internal administration of Yi kidney soup, selecting the foot Sanli, kidney acupoints and San Yin Jiao points, suggested that the method could effectively improve renal function-related indicators and slow down kidney damage. In addition, a systematic evaluation showed that acupoint injection therapy was relatively superior to acupuncture alone, probably because this method could better apply drug effects through the meridians to the organism [15].

3.3 Point-application

Point-application is equivalent to a form of transdermal drug delivery, and is used to prevent and treat diseases by identifying and selecting acupuncture points. Zhao Yuwu [16] et al used spleen-supplementing and kidney-supplementing soup combined with Chinese herbal acupuncture point patching (Qihai, Huanjiao, and Taixi points) to treat early and mid-stage DN, and after 4 weeks of treatment, The total effective rate of treatment in the observation group was 97.50%, and the patients' renal function improved significantly. Lei Bing [17] et al. treated patients with early DN with the same significant clinical efficacy and a decrease in the level of relevant inflammatory factors in patients based on conventional corresponding treatment with Chinese herbal internal medicine combined with Chinese herbal acupuncture point application (Qihai, Kidney Yu, Taixi, Yishe, Foot Sanli, Huanjiao and

Taichong points). Zhu Xuelei^[18] Eighty patients with type 2 diabetic nephropathy stage III-IV were selected and treated with the combination of Yi kidney eliminating turbidity and diuretic soup with point-application (lung acupoint, kidney acupoint, Guan Yuan, and foot San Li acupoints) on top of the symptomatic treatment of conventional low-salt and low-fat and sugar reduction in Western medicine for 4 weeks, and it was found that the kidney function-related indexes in the treatment group improved significantly and the TCM evidence points were smaller than those in the control group, indicating significant clinical efficacy.

3.4 Moxibustion Therapy

Moxibustion therapy is to prevent and cure diseases by burning moxibustion materials, burning and warming the diseased areas of the body, and conducting the drug action and warm stimulation through the meridians^[19]. Chen Yuling^[20] believed that the early stage of kidney disease is mostly due to spleen-kidney yang deficiency combined with blood stasis. 70 patients with DM early stage kidney disease with spleen-kidney yang deficiency were treated with moxibustion (Yongquan and Kidney Yu) combined with oral Chinese medicine formula, and the decrease in urine microalbumin and ACR were more obvious in the treated group after 8 weeks of treatment than in the conventional western medicine antihypertensive group. Zhu Dan^[21] et al used warm yang and kidney tonic moxibustion as an adjunct to the basic Western medicine treatment for DN patients, and the patients in the treatment group were better than the control group in terms of clinical efficacy, TCM evidence score, renal function index, cognitive dysfunction and self-management behavior score, which could effectively alleviate the progression of DN with significant effects. Shan Liufeng^[22] et al divided 80 patients with stage III DN into observation and control groups by random sampling method, and added moxibustion therapy to the control group on the basis of conventional treatment, and added warming kidney, tonifying qi and activating blood formula to the observation group on the basis of treatment in the control group, and after 4 weeks, the total efficiency of the observation group was significantly better than that of the control group, and the improvement of renal function index and meridian energy index in the observation group was significantly higher than that of the control group. The above indicates that moxibustion therapy combined with Chinese herbal medicine for DN is effective.

3.5 Chinese medicine enema therapy

Chinese medicine enema therapy is the rectal administration of Chinese medicine preparations by enema, which further penetrates and diffuses the drug to reach the disease, so that patients can increase the number of bowel movements, remove toxins, improve renal function and reduce urinary protein levels, and it is easy to operate and safe and effective. One of the systematic evaluations on the treatment of stage IV DN with Chinese herbal enemas suggested that the combination of western basic treatment with Chinese herbal enemas for patients with stage IV DN had significant advantages in terms of overall efficiency, reduction of relevant renal function indicators such as blood creatinine and urea nitrogen, and improvement of 24-h urinary protein levels^[23]. D. R. Ma^[24] et al divided 72 patients with stage IV DN into a control group (n=36) and a treatment group (n=36), and the treatment group applied rhubarb and aconite soup plus reduction enema twice a day in addition to diet, exercise, and western medicine basic treatment, and observed that the Chinese medicine evidence score and renal function decreased in both groups after 4 weeks, and the treatment group was significantly better than the control group ($P<0.05$), and the total effective rate of the treatment group was 91.6%, which was significantly better than the control group ($P<0.05$). The total efficiency of the treated group was 91.6%, which was significantly better than that of the control group ($P<0.05$), indicating that the enema with addition and subtraction of rhubarb and aconite soup could significantly improve the renal function of patients in the middle and late stages of DN. Ding Li^[25] Using the sugar kidney enema formula (rhubarb, calcined oyster, danshen, black shun tablets, zedoary, raw locust flower, scutellaria) to treat patients with stage III-IV DN, it was found that this method could effectively reduce urinary microalbumin levels in patients with stage III-IV DN, and the TCM symptom scores and efficacy ratings of the treatment group were significantly better than those of the control group, which could improve patients' symptoms.

3.6 Other therapies

A Guide^[26] In the introduction to the medicinal diet is also applicable to DN patients, such as yam lotus seed rice, carp red bean soup, etc, and traditional gong methods, such as fitness qigong six characters, can regulate qi and blood, internal organs, improve the patient's blood sugar, kidney

function, etc.; Taijiquan is suitable for patients with early DN, which can strengthen the spleen, tonify the kidneys, Shu meridians, regulate qi and blood, and improve patients' blood pressure, UAER, and urinary β 2-microglobulin; however, traditional gong methods need to pay attention to contraindications, and patients with serious cardiopulmonary disease, organism bleeding tendency, and overly deficient body should not use this method.

4. Conclusion

In recent years, most of the external therapies of TCM for DN are combined therapies, combined with Western basic therapy or internal administration of Chinese herbal medicine, with significant efficacy and easy clinical operation methods, and high patient acceptance, which are worthy of wide application. However, there are similar problems with TCM research, such as: low reliability of evidence-based medical evidence in clinical trials, small sample size, short duration, and imperfect protocol design; lack of unified classification and diagnostic criteria, as well as efficacy assessment criteria of TCM external treatment. Therefore, in the future, we should unify and standardize the criteria for assessing the efficacy of TCM external treatment, expand the sample size of studies, and establish randomized, double-blind controlled, multicenter clinical studies to provide a more adequate theoretical basis for clinical research and treatment.

References

- [1] Wang L, Peng W, Zhao Z, et al. Prevalence and Treatment of Diabetes in China, 2013-2018 [published correction appears in JAMA. 2022 Mar 15;327(11):1093]. JAMA. 2021; 326(24):2498-2506. doi:10.1001/jama.2021.22208
- [2] Zhang L, Long J, Jiang W, et al. Trends in Chronic Kidney Disease in China [J]. N Engl J Med, 2016, 375(9): 905-906.
- [3] Microvascular Complications Group of the Chinese Medical Association Diabetes Branch. Guidelines for the prevention and treatment of diabetic nephropathy in China (2021 edition) [J]. Chinese Journal of Diabetes, 2021, 13 (8):762-784.
- [4] Li F, Wang Qiuhong, Wei Junping. Clinical research progress of Chinese medicine in the treatment of diabetic nephropathy [J]. Medical Review, 2020, 26(17):3471-3475.
- [5] Li P, Li SHM, Cheng QS. Modern Chinese medicine nephrology [M]. Beijing: China Medical Science and Technology Press, 2021: 388-393.
- [6] Mo ZY, Liu CH, Xue SY, et al. Research progress on the pathogenesis and treatment of diabetic nephropathy [J]. Journal of localized surgery, 2021, 30(12):1093-1098.
- [7] Liu L, Dong Q. Y, Hao H, et al. Effects of "regulating spleen and stomach acupuncture" on the expression of PCX, CD2AP, nephrin and desmin in the foot cells of rats with type 2 diabetic nephropathy [J]. Journal of Changchun University of Traditional Chinese Medicine, 2023, 39(02):152-155.
- [8] Ye Z H, Gao M S, Hu Y W, et al. 50 cases of early diabetic nephropathy with deficiency of both qi and blood treated by combining acupuncture with Diqi and Blood Activation Soup[J]. Global Chinese Medicine, 2021, 14(10): 1893-1896.
- [9] Zhang HJ, Ding WK, Zhao DP, et al. Clinical study on vascular endothelial injury in diabetic nephropathy treated with needle and drug combination [J]. Liaoning Journal of Traditional Chinese Medicine, 2021, 48(5): 151-155.
- [10] Liu R P, Zhang S C. Clinical observation on the treatment of diabetic nephropathy with Yin and Yang deficiency by acupuncture with Jisheng Kidney Qi Pill[J]. Shanghai Journal of Acupuncture and Moxibustion, 2021, 40(2): 136-141.
- [11] Ding Y. Efficacy of Chinese medicine acupuncture point injection combined with warming spleen and tonifying kidney soup plus reduction in the treatment of diabetic nephropathy with internal blood stasis [J]. Hubei Journal of Traditional Chinese Medicine, 2019, 41(05):6-8.
- [12] Ji Z R. Clinical efficacy evaluation of ascending and descending san combined with acupoint injection on early diabetic nephropathy [J]. Tibetan Medicine, 2022, 43(03):147-149.
- [13] Zhao Cheng. Clinical study on the treatment of diabetic nephropathy by combining Yi kidney soup with self-blood acupoint injection [D]. Shandong University of Traditional Chinese Medicine, 2020.
- [14] Jia Ying. Systematic evaluation of acupuncture therapy for the treatment of diabetic nephropathy [D]. Zhejiang University of Traditional Chinese Medicine, 2019.
- [15] Zhao YW, Zhang GZ. Clinical efficacy of combining spleen and kidney tonics with Chinese herbal acupressure in the treatment of early and mid-stage diabetic nephropathy [J]. Inner Mongolia

Traditional Chinese Medicine, 2021, 40(09):63-64.

[16] Lei B, Huang HN, Liu YF, et al. Investigation of the effect of Chinese herbal medicine zhiyin tongluo soup combined with acupressure on the improvement of renal function in patients with early diabetic nephropathy[J]. *Journal of Jiangxi University of Chinese Medicine*, 2021, 33(02):37-39.

[17] Zhu Xuelei. Clinical efficacy observation of Yi kidney eliminating turbidity and diuretic soup combined with acupuncture point patching in the treatment of diabetic nephropathy stage III-IV [J]. *Sichuan Traditional Chinese Medicine*, 2019, 37(04):121-123.

[18] Liu YD, Meng XY, Cheng T, et al. Overview of the pathogenesis and treatment of diabetic nephropathy in Chinese and Western medicine[J]. *Western Traditional Chinese Medicine*, 2019, 32(07): 134-138.

[19] Chen Yuling. The efficacy of warming Yang and activating Blood method in treating early diabetic nephropathy of Spleen and Kidney Yang deficiency type [D]. Guangzhou: Guangzhou University of Traditional Chinese Medicine, 2019.

[20] Zhu D, Li LJ. Effect of warming yang and tonifying kidney moxibustion adjunctive therapy on patients with diabetic nephropathy [J]. *Liaoning Journal of Traditional Chinese Medicine*, 2022, 49(05): 176-179.

[21] Shan Liufeng, Meng Jingxi, Lu Liang. Effect of warming kidney, tonifying qi and activating blood formula combined with moxibustion on renal function and meridian energy index in patients with stage 3 diabetic nephropathy [J]. *World Journal of Integrative Chinese and Western Medicine*, 2022, 17(10): 2001-2005.

[22] Chen M-L, Sun L-Y, Sun W-W, et al. Systematic evaluation of Chinese medicine enema for stage IV diabetic nephropathy[J]. *Journal of Chinese Medicine*, 2020, 35(12):2706-2712.

[23] Ma DRE, Zhang Y, Huang SUM, et al. Clinical observation on the treatment of diabetic nephropathy by enema with rhubarb and eucommia soup [J]. *Asia-Pacific Traditional Medicine*, 2021, 17(06): 69-72.

[24] Ding L. Clinical efficacy of sugar kidney enema formula in patients with diabetic nephropathy stage III-IV combined with dyslipidemia [D]. Xinjiang Medical University, 2020.

[25] Yu JY, Ni Q, Liu Su. Guidelines for the combined treatment of diabetic nephropathy [J]. *Journal of Traditional Chinese Medicine*, 2022, 63(02):190-197.

[26] Sun Xiaolin. Effect of fitness qigong six-character technique on glucose metabolism and blood rheology in patients with diabetic nephropathy [J]. *Journal of Liaoning University of Traditional Chinese Medicine*. 2018, 20(7):148-151.