Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 8
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Clinical Study on the Treatment of Diabetic Retinopathy (Qi-Yin Deficiency Type) with the Method of Soothing the Liver, Harmonizing the Spleen, and Opening the Orifices

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Abstract: *Objective*: To observe the clinical efficacy of the method of softening the liver, harmonizing the spleen, and unblocking the orifices in the treatment of Xiaoke Neizhang with Qi and Yin deficiency type. *Methods*: Seventy-two patients with Xiaoke Neizhang of qi and yin deficiency type were selected from March 2024 to May 2025 and divided into a treatment group and a control group with 36 cases each according to the random number table method. The treatment group was treated with the method of softening the liver, harmonizing the spleen, and unblocking the orifices, which included oral administration of Softening the Liver and Harmonizing the Spleen Pills combined with iontophoresis of Xuesaitong Injection. The control group was treated with oral administration of calcium dobesilate capsules. Both groups were treated for 2 courses, and multiple indicators such as visual acuity, fundus condition, and TCM syndrome scores were compared between the two groups. *Results*: The total effective rate of the treatment group was higher than that of the control group. There were significant differences in visual acuity, fundus condition, and TCM syndrome scores between and within the groups ($P < 0.05$). *Conclusion*: The method of softening the liver, harmonizing the spleen, and unblocking the orifices has a definite clinical effect in the treatment of Xiaoke Neizhang with Qi and Yin deficiency type. It has a direct effect, is painless, easy for patients to accept, and has high clinical application value.

Keywords: Softening the Liver and Harmonizing the Spleen Pills; Xuesaitong injection; Iontophoresis; Xiaoke Neizhang; Qi and Yin deficiency type

Online publication: August 19, 2025

1. Introduction

Diabetic retinopathy, known as "Xiaoke Neizhang" in Chinese medicine, is considered one of the most common complications of diabetes. The longer the duration of diabetes and the more significant fluctuations in blood sugar levels, the higher the risk of developing this disease. It has become one of the leading causes of blindness in China and has severely impacted people's learning and quality of life. Currently, Western medicine offers various treatments for this condition, such as oral medications, drug injections, vitrectomy, or laser surgery. The clinical efficacy of different treatment methods varies. In contrast, traditional Chinese medicine (TCM) takes a holistic approach, emphasizing syndrome differentiation and treatment, and adopts a combination of internal and external therapies. This approach leverages the strengths of TCM to effectively delay the progression of the disease. This article observes the clinical efficacy of the "soft liver and spleen-opening therapy" for Xiaoke Neizhang with deficiency of both qi and yin. The research results are reported below:

2. Materials and methods

2.1. General Information

This study selected 72 patients diagnosed with Xiaoke Neizhang (deficiency of both qi and yin) at the ophthalmology clinic and inpatient department of our hospital from March 2024 to May 2025. The patients were randomly divided into a treatment group and a control group using a random number table method, with 36 patients in each group. The treatment group consisted of 20 males and 16 females, aged between 31 and 65 years (mean age: 54.00 ± 9.02 years), with a disease duration of 10.56 ± 6.70 years. The control group consisted of 22 males and 14 females, aged between 33 and 65 years (mean age: 53.28 ± 8.13 years), with a disease duration of 10.61 ± 7.45 years. There was no statistically significant difference in general information between the two groups ($P > 0.05$). This study was approved by the hospital's medical ethics committee (Changzhonglunshen [2023] No. 003), and all subjects were informed of the study content and signed informed consent forms before treatment.

2.2. Inclusion criteria

(1) Diagnosis of diabetic retinopathy with Qi and Yin deficiency syndrome, referring to "National Higher Education '14th Five-Year Plan' Textbook for the Traditional Chinese Medicine Industry" edited by Peng Qinghua [2].

(2) Age between 30 and 65 years old.

(3) No severe cardiac, cerebral, or psychiatric diseases.

(4) Signed "informed consent" can be included in the observation cases.

2.3. Exclusion criteria

(1) Age below 30 or above 65 years old.

(2) Severe cardiac, cerebral, or psychiatric diseases.

(3) Occurrence of serious adverse events.

(4) Development of severe comorbidities during the trial.

(5) Failure to meet the inclusion criteria or inability to follow prescribed treatment that affects efficacy evaluation.

2.4. Methods

2.4.1. Treatment methods

Both groups of patients received conventional hypoglycemic therapy.

(1) Treatment group: Adopting the method of softening the liver, harmonizing the spleen, and clearing the orifices, specifically using Softening Liver and Harmonizing Spleen Pills (Changchun Traditional Chinese Medicine Hospital, production batch number 230501), 1 pill per day taken orally; combined with Xuesaitong Injection (Heilongjiang Zhenbaodao Pharmaceutical Co., Ltd., production batch number A07220708079) for iontophoresis: 4ml of the medicinal solution was used to soak a gauze pad, which was then wrapped around the electrodes and placed on both eyes, connected to the cathode; the auxiliary electrode was wrapped in a saline-soaked gauze and placed on the wrist, connected to the anode. The current intensity was controlled at 10-15mA, with each treatment session lasting 20 minutes, once per day.

(2) Control group: Administered with Calcium Dobesilate Capsules (0.5g/capsule, Shanghai Zhaohui Pharmaceutical Co., Ltd.), 1 capsule taken three times per day orally.

(3) Observation period: Continuous treatment for 2 courses, with each course lasting 10 days, totaling 20 days.

2.4.2. Observation indicators

(1) Vision loss: 3 points for corrected vision decreasing to below 0.1, 2 points for decreasing to 0.1–0.25, and 1 point for decreasing to 0.3–0.6.

(2) Retinal hemorrhage: 3 points if hemorrhage is present in all four quadrants of the retina, 2 points if hemorrhage is seen in two to three quadrants, and 1 point if hemorrhage is only present in one quadrant.

(3) Visual field obstruction: 3 points for complete visual field obstruction, 2 points for 1/2 visual field obstruction, and 1 point for 1/4 visual field obstruction.

2.4.3. Therapeutic effect evaluation

Referring to the "Guiding Principles for Clinical Research of New Chinese Medicines" from 2002 the below are as follow [1]:

(1) Markedly effective: Vision improves by more than 4 rows, with vision no less than 1.0. Fundus examination shows a reduction or disappearance of microaneurysms; the amount of fundus hemorrhage decreases by one grade or disappears completely; and exudation also decreases by one grade or disappears. If two of these three criteria are met, it is considered markedly effective.

(2) Effective: Vision improves by 2 to 3 rows, and the number of microaneurysms decreases by one grade; both the amount of fundus hemorrhage and the amount of exudation decrease by one grade. If one of these three criteria is met, it is considered effective.

(3) Ineffective: None of the three criteria are met.

2.4.4. Statistical methods

Data analysis was performed using SPSS (26.0) statistical software. Measurement data were expressed as mean ± standard deviation ($\overline{x} \pm s$), and comparisons between and within groups were performed using the t-test. Count data were expressed as rates, and a P-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of overall therapeutic effect between the two groups

The total effective rate of the treatment group was higher than that of the control group. After χ^2 test, $P < 0.05$, indicating a statistically significant difference (**Table 1**).

Table 1. Comparison of clinical total effective rate between the two groups [n(%)]

Group	Cases (n)	Markedly Effective n (%)	Effective n (%)	Ineffective n (%)	Total Efficacy (%)	χ^2	*P*-value
Treatment	36	13	20 (55.6)	3	91.7	6.651	0.036
Control	36	5	22	9	75.0		

3.2. Comparison of visual acuity between the two groups

After treatment, the visual acuity of both groups was higher than before treatment, and the visual acuity of the treatment group was higher than that of the control group. After t-test, $p < 0.05$, indicating a statistically significant difference (**Table 2**).

Table 2. Comparison of visual acuity between the two groups

Group	*n*	Pre-treatment	Post-treatment	*p*-value
Treatment	36	0.44 ± 0.03	0.68 ± 0.03	< 0.01
Control	36	0.45 ± 0.03	0.54 ± 0.03	< 0.01
t-value	-	-0.16	2.84	-
p-value	-	0.89	0.006	-

3.3. Comparison of fundus conditions between the two groups

After treatment, the values of various indicators of fundus conditions in both groups were lower than before treatment, and the treatment group was lower than the control group. $P < 0.05$, indicating a statistically significant difference (**Table 3**).

Table 3. Comparison of fundus conditions between the two groups

Group	*n*	Microaneurysms (count)		Hemorrhage (mm²)		Exudates (mm²)	
		Pre- treatment	Post- treatment	Pre- treatment	Post- treatment	Pre- treatment	Post- treatment
Treatment	36	11.2 ± 4.1	8.7 ± 2.6	0.14 ± 0.05	0.11 ± 0.03	0.06 ± 0.04	0.04 ± 0.02
Control	36	11.0 ± 3.9	9.6 ± 3.1	0.19 ± 0.03	0.17 ± 0.02	0.06 ± 0.04	0.05 ± 0.03
t-value	-	0.164	3.032	0.164	3.561	0.014	2.957
p-value	-	0.763	0.004	0.735	< 0.01	0.927	0.007

3.4. Comparison of TCM syndrome scores between the two groups

After treatment, the scores of traditional Chinese medicine (TCM) syndromes in both groups were lower than before treatment, and the scores of TCM syndromes in the treatment group were lower than those in the control group, with $p < 0.05$ indicating a statistically significant difference (**Table 4**).

Table 4. Comparison of TCM syndrome scores between the two groups

Group	n	Baseline	Post-treatment	*t*-value	*p*-value
Treatment	36	8.78 ± 2.34	4.39 ± 1.84	16.94	< 0.001
Control	36	8.64 ± 2.90	8.36 ± 2.96	9.94	0.006
t-value	-	0.22	-6.84	-	-
p-value	-	0.82	< 0.001	-	-

4. Discussion

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia caused by multiple etiologies. Long-term carbohydrate, fat, and protein metabolism disorders in diabetes can cause multisystem damage, such as chronic progressive damage, functional decline, and failure of tissues and organs like eyes, kidneys, nerves, heart, and blood vessels [3]. In traditional Chinese medicine, diabetes is categorized as "Xiaoke" (wasting-thirst syndrome). Retinopathy is a common complication of this disease, with symptoms such as decreased vision, visual obstruction, or visual distortion. In severe cases, it can lead to vision loss. Western medicine refers to it as diabetic retinopathy. The prevalence of this disease is as high as 54% among patients with a history of diabetes ranging from 5 to 15 years. It is gradually becoming younger and is the leading cause of blindness among the working population. In traditional Chinese medicine, diabetic retinopathy is known as "Xiaoke Neizhang" or "Xiaoke Mubing". Based on etiology and pathogenesis, it is clinically classified into other syndromes such as Qi and Yin deficiency, spleen and kidney deficiency, Yin deficiency with stagnation, and phlegm and blood stasis obstruction [1]. This study focuses on patients with Qi and Yin deficiency type of Xiaoke Neizhang.

In Western medicine, the early treatment of diabetic retinopathy mainly involves oral medication. In the middle and late stages, retinal laser photocoagulation, vitrectomy, and other methods are used based on the condition of the ocular fundus. However, the recovery of retinal function after surgery is often unsatisfactory. For patients with macular edema or retinal neovascularization, anti-VEGF therapy is commonly used, which requires long-term and multiple treatments. Due to the high cost of treatment, it is difficult for patients to adhere to it, thus affecting the clinical efficacy.

The treatment of this disease in traditional Chinese medicine starts from the "holistic concept and syndrome differentiation and treatment", and there are many treatment methods, such as traditional Chinese medicine decoction, external treatment methods such as iontophoresis or acupuncture, combined Chinese and Western medicine treatment, and combined traditional Chinese medicine and laser treatment. Especially after retinal laser surgery or vitrectomy combined with traditional Chinese medicine therapy, it can consolidate the clinical efficacy and reduce the recurrence rate of the disease.

The method of softening the liver, harmonizing the spleen, and opening the orifices is a treatment approach established based on the basic theories of traditional Chinese medicine and the five-wheel theory of ophthalmology in traditional Chinese medicine. This method connects the eyes with the internal organs, focusing on analyzing local symptoms and combining them with systemic disorders for dialectical treatment. This study involves both internal and external treatment, specifically oral administration of Softening Liver and Harmonizing Spleen Pills combined with iontophoresis using Xuesaitong injection.

Softening Liver and Harmonizing Spleen Pills are a preparation made in our hospital and have been used for

more than 60 years. It has the effect of strengthening the spleen and stomach, dispersing liver Qi, and regulating Qi. The formula consists of Chai Hu (Bupleurum), Bai Shao (White Peony), Chao Bai Zhu (Fried Atractylodes), Chao San Xian (Fried Three Immortals), and other medicinal herbs. Chai Hu has the effect of dispersing liver Qi stagnation and elevating Yang Qi. It contains multiple components, such as saikosaponin, which have strong anti-inflammatory effects, can reduce the secretion of various inflammatory mediators, reduce the degree of retinal inflammation, protect the existing barrier function of the blood-retinal barrier, thereby effectively improving blood vessel permeability and preventing retinal edema or obvious exudation. Bai Shao nourishes the liver and blood, relieves pain, and contains components such as paeoniflorin, which have a protective effect on the optic nerve.

At the same time, it has a good effect on the expansion of eye blood vessels, can significantly reduce the blood viscosity in the area, improve microcirculation, deliver nutrients to various retinal cells, and thereby improve retinal metabolism. Chai Hu and Bai Shao are the most classic herbal pair for dispersing liver Qi stagnation and regulating emotions. They are used frequently in classical prescriptions. The combination of the two can not only disperse liver Qi stagnation but also nourish the liver and blood, possessing both dispersing and converging functions, and can nourish the liver and nourish Yin [4]. Baizhu (*Atractylodes macrocephala*) has a bitter, sweet, and warm taste, attributed to the spleen and stomach meridians. It has the effect of strengthening the spleen, nourishing Qi, drying dampness, and promoting urination. Baizhu can be used raw or fried. The selection of fried Baizhu can reduce its drying property, decrease gastrointestinal irritation, and enhance its spleen-strengthening effect. “Fried Sanxian” includes fried Shenqu (fermented mass of wheat, etc.), fried malt, and fried hawthorn. “Fried Sanxian” is chosen instead of “Jiao Sanxian” because frying is more suitable for strengthening the spleen and promoting digestion. Considering the meridian attributes of all the herbs in the formula, it can be attributed to the liver, spleen, and stomach meridians.

External treatment is based on internal treatment and combined with the iontophoresis of Chinese herbal medicines. Iontophoresis has a long history of application. It utilizes the characteristics of direct current to rapidly and fully introduce drug ions into the tissue. Simultaneously, combined with external electric field driving, it can precisely introduce drug ions into specific areas. Xuesaitong injection, which mainly contains Panax notoginseng saponins, is selected for its excellent hemostatic effect, as well as its ability to resolve blood stasis and reduce swelling. In this study, Xuesaitong injection is used externally directly on the eyes to enhance the local drug concentration. This method has the advantages of direct action and fast onset. It allows the drug to act directly on the eyes without passing through the bloodstream, resulting in higher safety benefits after administration. Effective stimulation of multiple acupoints around the eyes can regulate blood circulation in the area, enabling the full absorption of nutrients. Therefore, it can improve visual function and is well-accepted by patients.

5. Conclusion

In summary, this study adopts a method that treats both the liver and spleen simultaneously, addressing both the symptoms and root causes. This approach fully demonstrates the advantages of combined therapy targeting both qi and blood, as well as the organs. Through clinical observation of 72 patients with diabetic retinopathy, it was found that compared to simply taking calcium dobesilate capsules orally, the combined therapy can improve patients’ vision and ameliorate retinal hemorrhage and macular edema. During follow-up visits at 1, 3, and 6 months after treatment, it was observed that patients’ vision and retinal conditions remained stable, effectively controlling the further progression of the disease. For patients who have undergone vitrectomy or retinal photocoagulation

surgery, traditional Chinese medicine therapy can alleviate post-surgical retinal edema symptoms and consolidate the surgical effect. For patients receiving anti-VEGF therapy for macular edema, this therapy can prolong the duration of intraocular injection treatment and reduce the burden on patients. Traditional Chinese medicine therapy plays an irreplaceable role in improving vision, retinal conditions, and optic nerve protection. It can also improve retinal microcirculation, promote the absorption of retinal hemorrhage and macular edema, and reduce the blindness rate. This therapy serves as a complement to Western medical treatments, and the combination of Chinese and Western medicine effectively delays disease progression.

Funding

2024 Scientific Research Project of Jilin Provincial Administration of Traditional Chinese Medicine (Project No.: 2024139)

Disclosure statement

The authors declare no conflict of interest.

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