ISSN: 3033-3512

Journal of Traditional Medicine and Chinese Medicine

SCIENTIFIC Research and Community

Research Article

Open Access

A Controlled Clinical Study on Efficacy and Safety of Qi-Zhi-Yi-Shen Formula in Treating Qi Deficiency and Blood Stasis Syndrome in Chronic Glomerulonephritis

Yu Sun[1,2#], Yuye Li[1,2#], Yan Shi[1], Qingsi Wen[1], Qingnan Zhu[1,2], Zewen Yan[1], Shuwei Ren[1,2], Xiangbo Qi[1,2], Maomao Wu[1] ,Jianguo Xie[1*] and Dapeng Wang[1,2*],

[1]College of Integrated Traditional Chinese and Western Medicine, Dalian Medical University, Liaoning Dalian 116044, China

[2]The First Affiliated Hospital of Dalian Medical University, Liaoning Dalian 116011, China

ABSTRACT

Objective

Evaluate the clinical efficacy and safety of Qi-Zhi-Yi-Shen Formula in treating qi deficiency and blood stasis syndrome in chronic glomerulonephritis (CGN).

Methods

The clinical study included 48 patients with qi deficiency and blood stasis type chronic glomerulonephritis, who were divided into an experimental group and a control group based on actual conditions and patient willingness, receiving treatment for 8 weeks. Both groups underwent routine basic treatment; the control group received conventional treatment supplemented with Irbesartan tablets, while the experimental group additionally received modified Qi-Zhi-Yi-Shen Formula. Relevant indicator data were collected to assess changes in urinary protein quantification, kidney function indicators, urinary red blood cell count, and traditional Chinese medicine syndrome scores before and after treatment. Statistical analysis of all data was performed using SPSS software to compare the differences in results within and between groups before and after treatment.

Results

Before treatment, the basic information and various indicators of both groups were comparable ($P > 0.05$). After treatment, comparisons showed: ① 24-hour urinary protein quantification: both groups showed significant improvement ($P < 0.05$), with the experimental group outperforming the control group ($P < 0.05$). ② Urinary red blood cell count: both groups improved compared to before ($P < 0.05$), with the experimental group outperforming the control group ($P < 0.05$). ③ Creatinine: both groups had lower creatinine levels compared to before ($P < 0.05$), with the experimental group outperforming the control group ($P < 0.05$). ④ Traditional Chinese medicine syndrome scores: both groups showed a decrease ($P < 0.05$), with the experimental group outperforming the control group ($P < 0.05$). ⑤ Overall efficacy comparison: the total effective rate of the experimental group was 95.8%, while that of the control group was 83.3%. ⑥ Comparison of traditional Chinese medicine syndrome efficacy: the effective rate of the experimental group was 95.8%, while that of the control group was 83.3%. No abnormal blood potassium levels or liver function damage occurred during treatment.

Conclusion

The application of Qi-zhi-Yi-shen Formula on the basis of conventional Western medicine treatment can significantly improve the traditional Chinese medicine syndrome scores, kidney function indicators, urinary protein quantification, and urinary red blood cell count in patients with chronic glomerulonephritis, with good safety.

#Co-first author

***Corresponding author**

Dapeng Wang, College of Integrated Traditional Chinese and Western Medicine, The First Affiliated Hospital of Dalian Medical University, Liaoning Dalian 116011, China. E-mail: bobowdp@163.com

Jianguo Xie, College of Integrated Traditional Chinese and Western Medicine, Dalian Medical University, Liaoning Dalian 116044, China , E-mail: DLxjguo2016@163.com.

Received: July 10, 2025; **Accepted:** July 15, 2025; **Published:** July 25, 2025

Keywords: Chronic Glomerulonephritis, Qi-Zhi-Yi-Shen Formula, Clinical Efficacy Observation

Introduction

Chronic glomerular nephritis (CGN) is primarily characterized by proteinuria, hematuria, edema, and hypertension, and can ultimately progress to chronic kidney disease (CKD) or end-stage renal disease (ESRD). In China, CGN remains the leading cause of ESRD. Therefore, in the treatment of CGN, it is of great significance to delay the progression of kidney function, postpone the timing of renal replacement therapy, and improve the quality of life of patients [1,2].

The pathogenesis of CGN involves multiple complex pathological processes. Studies suggest that its etiology may be related to infections, immune imbalance, genetic factors, and other diseases. The pathological mechanisms may involve several aspects: the deposition of immune complexes leading to inflammatory reactions, renal fibrosis, and damage to renal intrinsic cells. Various factors interact, ultimately leading to the occurrence and progression of the disease. Currently, Western medicine's treatment plans for CGN still focus on symptomatic treatments such as glucocorticoids, renin-angiotensin system (RAS) inhibitors, immunosuppressants, cytotoxic drugs, and diuretics. However, the clinical application of glucocorticoids or cytotoxic drugs often involves long treatment courses and significant side effects, and their active use is generally not recommended. RAS inhibitors can dilate the afferent arterioles, reduce intraglomerular pressure, and alleviate the hyperfiltration state of the glomeruli, thus helping to reduce proteinuria, lower blood pressure, and protect the kidneys. Although their safety is superior to that of glucocorticoids, long-term use of such drugs may increase the risk of kidney function damage, especially in patients whose blood pressure or kidney function is highly dependent on the RAS, where RAS may induce hemodynamic disturbances, further affecting kidney function recovery [3-10].

In recent years, traditional Chinese medicine (TCM) has increasingly demonstrated its unique advantages in the treatment of CGN, gradually playing an important role in delaying the timing of renal replacement therapy, improving hematuria and proteinuria levels, and reducing complications. Ancient medical texts do not record a specific name for CGN; instead, it is categorized based on clinical manifestations of proteinuria and hematuria as "kidney wind," "urinary turbidity," "edema," etc. It is currently recognized that the pathogenesis of this disease is often due to deficiency of the lung, spleen, and kidney, combined with wind-cold, damp-heat, and blood stasis. "Water is the most yin; its root is in the kidney, its manifestation is in the lung, and its regulation is in the spleen." The kidney governs water and controls the body's fluids, while also having the function of consolidating qi, blood, and essence. Insufficient consolidating power leads to hematuria and proteinuria; the lung disseminates and regulates the water pathways; the spleen governs transportation and transformation, and if the spleen is deficient and weak, it cannot transform and transport dampness. Congenital deficiency of the kidney and acquired malnutrition of the spleen lead to qi deficiency of the spleen and kidney, resulting in insufficient blood circulation and blood stasis. Blood stasis and dampness obstruct and stagnate, blocking the kidney collaterals, ultimately evolving into accumulations. Professor Wang Yongjun advocates that the treatment of CGN should start from the perspectives of deficiency, stasis, and wind-damp, with treatment focusing on adjusting the yin-yang, qi, and blood of the kidney, using methods to tonify deficiency, unblock collaterals, eliminate stasis, and resolve accumulations, and finally expel wind and eliminate dampness to clear the source and rectify the foundation. Professor Wang Dapeng, through long-term clinical practice, has found that CGN patients often present with qi deficiency and blood stasis syndrome, thus adopting the general principle of invigorating qi, activating blood, and unblocking collaterals, innovatively selecting Astragalus 40g, Hirudo 10g, and Tripterygium wilfordii 20g to form the Qi-Zhi-Yi-Shen formula. Research has found that Astragalus has the functions of benefiting qi, consolidating the exterior, nourishing blood, promoting muscle regeneration, and diuresis. Astragaloside IV, as a major component of Astragalus, has protective effects on acute kidney injury caused by sepsis, renal ischemia-reperfusion injury, and diabetic nephropathy. "Hirudo does not harm new blood, and the qi aspect remains intact; blood stasis dissipates without a trace," indicating its strong ability to break blood stasis and unblock meridians. The main component hirudin can inhibit coagulation and impede thrombus formation, exhibiting anti-inflammatory effects and improving kidney function. Vine-like medicinal herbs are characterized by their expansive and spreading forms, possessing the property of dispersing with pungent and aromatic qualities, effectively expelling wind, unblocking collaterals, and eliminating accumulations. Tripterygium wilfordii expels wind-damp, unblocks meridians, and promotes urination, with its main components such as tripterygium glycosides having immunosuppressive effects and reducing proteinuria, inhibiting podocyte injury, and protecting the kidneys. Poria has diuretic and anti-edema effects, while licorice and platycodon have heat-clearing, detoxifying, phlegm-resolving, and throat-soothing properties. Their main components, poria acid, glycyrrhizic acid, and platycodon saponin D, have anti-inflammatory effects and inhibit oxidative stress, thereby reducing kidney damage. Typha angustifolia can inhibit platelet aggregation and promote fibrinolysis, having the effect of activating blood and resolving stasis, while its charred form has strong hemostatic properties. Epimedium strengthens kidney yang and expels wind-damp, with its main component icariin improving renal fibrosis. Thus, the Qi-Zhi-Yi-Shen formula is of great significance in the treatment of CGN, and this study aims to observe the clinical efficacy and safety of the Qi-Zhi-Yi-Shen formula in treating qi deficiency and blood stasis type CGN, hoping to provide new ideas and references for the clinical treatment of CGN [11-25].

Materials and Methods

Study Subjects

Patients with CGN who visited the outpatient and inpatient departments of the Nephrology Department at the First Affiliated Hospital of Dalian Medical University from October 2023 to November 2024 were collected and screened according to the inclusion criteria. This study has been approved by the hospital's ethics committee and has obtained the review approval document (Project No.: PJ-KS-KY-2024-712(X)).

Participants

Patients with qi deficiency and blood stasis syndrome CGN who visited the Nephrology Department outpatient and inpatient services of the First Affiliated Hospital of Dalian Medical University from October 2023 to November 2024 were selected. Based on clinical symptoms and patient willingness, the included patients were divided into the experimental group and the control group, with 24 cases in each group. The control group consisted of 11 males and 13 females; ages ranged from 24 to 68 years, with an average of (48.58±11.9) years. The experimental group included 14 males and 10 females; ages ranged from 22 to 79 years, with an average of (49.33±14.34) years. There was no statistically significant difference in general information between the two groups ($P>0.05$), indicating comparability. Inclusion criteria: (1) Meet the diagnostic criteria for CGN in the 10th edition of "Internal Medicine"; (2) Meet the diagnostic criteria for CGN in the "Guidelines for Clinical Research on New Chinese Medicines",with syndrome differentiation as qi deficiency and blood stasis syndrome. Main symptoms: lumbar and spinal pain, fatigue, or edema, reduced appetite or abdominal distension; secondary symptoms: loose stools, frequent urination or nocturia, pale red tongue with teeth marks, thin white coating, and thin pulse. Marked symptoms: dark or dull complexion; fixed or stabbing lumbar pain; purple or dark tongue with petechiae or ecchymosis; skin and nail changes or limb numbness, with a thin and rough pulse. At least two main symptoms, one secondary symptom, and at least one marked symptom must be present; (3) No gender restrictions, age range 18 to 80 years; (4) Voluntarily participating in this study and signing an informed consent form. Exclusion criteria: (1) Use of hormones, immunosuppressants, or renal replacement therapy

within the past three months; (2) Pregnant or breastfeeding women; (3) Comorbidities with other serious diseases such as cardiovascular, liver, or hematological disorders; (4) Allergic to the components of the study medication. The study was approved by the Ethics Committee of the First Affiliated Hospital of Dalian Medical University, and patients signed informed consent forms [26,27].

Interventions

Patients in the control group received treatment to control blood pressure, correct metabolic disorders, and were guided to follow a high-quality low-protein, low-salt diet, while also receiving oral treatment with Irbesartan tablets (Han Hui Pharmaceutical Co., Ltd., National Drug Approval No. H20000516, specification: 0.075g/tablet), 0.075-0.15g per dose, once daily. Patients in the experimental group received the Qi Zhi Yi Shen Fang treatment in addition to the control group treatment, with the formula: Astragalus 40g, Hirudo 10g, and Tripterygium wilfordii 20g. If edema was present, Poria 30g was added; if hematuria was present, Typhae pollen carbon 15g was added; for dry mouth, throat pain, or tonsillitis, Platycodon 15g and Glycyrrhiza 6g were added; for significant chills, Epimedium 15g was added. 100ml per dose, taken warm twice daily. Both groups of patients were treated for 8 weeks.

Outcomes

The primary outcome indicators include efficacy indicators, safety indicators, Traditional Chinese Medicine Syndrome Scoring (TCM), and Efficacy Assessment Criteria. Among them, the efficacy indicators mainly include 24-hour urinary protein quantification (24hUpro), urinary red blood cell count (URBC), and serum creatinine (Scr); the safety indicators mainly include liver function indicators such as alanine transaminase, aspartate transaminase (ALT, AST), etc., and serum potassium ion (K+); the TCM syndrome scores mainly involve observing changes in patients' low back pain, fatigue, or edema, dark or dull complexion, loose stools, frequent urination or nocturia, skin and nail changes or limb numbness, etc. Use a scoring method to indicate the severity: mild 1 point; moderate 2 points; severe 3 points. Tongue and pulse are recorded but not scored; specific scoring table can be found in the appendix. The Efficacy Assessment Criteria refer to the "Guidelines for Clinical Research on New Chinese Medicines", as detailed in Tables 1 and 2.

Table 1: Clinical Efficacy Assessment Criteria

Grade	Standard
Clinical Control	24hUpro Normal, Urbc Normal, Renal Function Normal
Significant Effect	24hUpro Reduced by ≥40%, URBC Reduced by ≥40%, Renal Function Basically Normal
Effective	24hUpro Reduced by <40%, URBC Reduced by <40%, Renal Function Normal or Improved
Ineffective	No Improvement or Worsening in Clinical Manifestations and Laboratory Tests

Table 2: Traditional Chinese Medicine Syndrome Efficacy Assessment Criteria

Grade	Standard
Clinical Cure	Clinical Symptoms and Signs Disappear or Are Basically Gone, Symptom Score Reduced by ≥95%
Significant Effect	Clinical Symptoms and Signs Significantly Improve, Symptom Score Reduced by ≥70%
Effective	Clinical Symptoms and Signs Show Improvement, Symptom Score Reduced by ≥30%
Ineffective	No Significant Improvement in Clinical Symptoms and Signs, Symptom Score Reduced by <30%

Note: The Calculation Formula is ([Pre-Treatment Score - Post-Treatment Score] ÷ Pre-Treatment Score) × 100%.

Statistical Analyses

Data were processed using SPSS 29.0. Chi-square tests were used for comparisons of count data between groups; normally distributed measurement data were expressed as ±s, with paired sample t-tests for intra-group comparisons and independent sample t-tests for inter-group comparisons; skewed distribution measurement data were described in the form of M(P25,P75), with paired sample rank sum tests for intra-group comparisons and two independent sample rank sum tests for inter-group comparisons; $P<0.05$ was considered statistically significant.

Results

Case Collection

A total of 54 cases were included in this study. Among them, the experimental group had 24 cases, with 5 dropouts (3 due to failure to return for follow-up on time, 2 excluded due to allergic reactions); the control group had 24 cases, with 1 dropout (due to switching to hormone treatment); the overall dropout rate was 11.1%. A total of 48 valid cases were collected, with 24 in the experimental group and 24 in the control group.

General Information

Comparison of Gender Composition Between Two Groups

Each group had 24 patients, with 14 males and 10 females in the experimental group; 11 males and 13 females in the control group. There was no statistical difference in gender composition between the two groups ($P > 0.05$), data are comparable, see Table 3.

Table 3: Comparison of Gender Between Two Groups (cases)

Group	Number of Cases (n)	Male (n,%)	Female (n,%)	t	P
Experimental Group	24	14 (58.3) %	10 (41.7) %	-0.858	0.391
Control Group	24	11 (45.8) %	13 (54.2) %		

Comparison of Age Between Two Groups

The average age of the experimental group was 49.33 ± 14.34 years, and the average age of the control group was 48.58 ± 11.9 years. There was no statistical difference in age between the two groups ($P > 0.05$), data are comparable, see Table 4.

Table 4: Comparison of Age Between Two Groups (years)

Group	Number of Cases (n)	Average Age (years)	t	P
Experimental Group	24	49.33±14.34	0.197	0.845
Control Group	24	48.58±11.9		

Efficacy Analysis

Comparison of 24hUpro Between the Two Groups

Inter-group comparison: There was no statistical difference in 24hUpro between the two groups before treatment ($P > 0.05$), and the data were comparable. After treatment, there was a statistically significant difference in 24hUpro between the two groups ($P < 0.05$).

Intra-group comparison: After treatment, 24hUpro decreased in both groups compared to before, with a statistically significant difference ($P < 0.05$), as detailed in Table 5.

Table 5: Comparison of 24hUpro Between the Two Groups [g/24h, M(P25,P75)]

Group	Experimental Group (n=24)	Control Group (n=24)	z	P1
Before Treatment	0.750.281.13	0.370.250.78	-1.608	0.108
After Treatment	0.240.130.56	0.370.250.75	-2	0.045
z	-4.286	-2.001		
P_2	0.001	0.045		

Note: P1 represents inter-group comparison, P2 indicates intra-group comparison at different time points.

Comparison of URBC Between the Two Groups

Inter-group comparison: There was no statistical difference in URBC between the two groups before treatment ($P > 0.05$), and the data were comparable. After treatment, there was a statistically significant difference in URBC between the two groups ($P < 0.05$).

Intra-group comparison: After treatment, URBC decreased in both groups compared to before ($P < 0.05$), with a statistically significant difference ($P < 0.05$), as detailed in Table 6.

Table 6: Comparison of URBC Between the Two Groups [uL, M(P25,P75)]

Group	Experimental Group (n=24)	Control Group (n=24)	z	P1
Before Treatment	11.15.2344.18	25.42.273.68	-0.65	0.516
After Treatment	6.153.1811.23	187.8535.4	-2.269	0.023
z	-3.4	-2.4		
P_2	0.001	0.016		

Note: P1 represents inter-group comparison, P2 indicates intra-group comparison at different time points.

Comparison of Scr levels Between the Two Groups

Inter-group comparison: There was no statistical difference in Scr between the two groups before treatment ($P > 0.05$), and the data were comparable. After treatment, there was a statistically significant difference in Scr between the two groups ($P < 0.05$).

Intra-group comparison: After treatment, Scr decreased in both groups compared to before, with a statistically significant difference ($P < 0.05$), as detailed in Table 7.

Table 7: Comparison of Scr Between the Two Groups [umol/L, ±s/M(P25,P75)]

Group	Experimental Group (n=24)	Control Group (n=24)	z	P1
Before Treatment	76.96±20.8	79 (62.25, 91.25)	-0.134	0.893
After Treatment	65.5 (58, 70.75)	75 (61, 90)	-1.991	0.046
z	-2.983	-2.017		
P_2	0.003	0.044		

Note: P1 represents inter-group comparison, P2 indicates intra-group comparison at different time points.

Comparison of Traditional Chinese Medicine Syndrome Scores Between the Two Groups

Inter-group comparison: There was no statistical difference in Traditional Chinese Medicine syndrome scores between the two groups before treatment ($P > 0.05$), and the data were comparable. After treatment, there was a statistically significant difference in Traditional Chinese Medicine syndrome scores between the two groups ($P < 0.05$).

Intra-group comparison: After treatment, Traditional Chinese Medicine syndrome scores decreased in both groups compared to before, with a statistically significant difference ($P < 0.05$), as detailed in Table 8.

Table 8: Comparison Of Traditional Chinese Medicine Syndrome Scores Between the Two Groups [points, ±s/M(P25,P75)]

Group	Experimental Group (n=24)	Control Group (n=24)	*t*	*z*	P_1
Before Treatment	26.67±2.41	27.42±2.34	-1.095	-	0.279
After Treatment	13 (12.25, 15)	1615,17	-	-3.895	<0.001
z	-4.3	-4.297			
P2	<0.001	<0.001			

represents inter-group comparison, P2 indicates intra-group comparison at different time points.

Clinical Efficacy

After treatment, the total effective rate of the experimental group was 95.8%, while that of the control group was 83.3%. The rank-sum test yielded Z=-3.883, P<0.001, indicating a statistically significant difference, as detailed in Table 9.

Table 9: Comparison of Clinical Efficacy Between the Two Groups (n, %)

Group	Clinical Cure/Cases (%)	Significant Effect/ Cases (%)	Effective/Cases (%)	Invalid/Cases (%)	Total Effective Rate (%)
Experimental Group (n=24)	5 (20.8%)	10 (41.7%)	8 (33.3%)	1 (4.2%)	95.8%
Control Group (n=24)	1 (4.2%)	0	19 (79.2%)	4 (16.7%)	83.3%

Efficacy of Traditional Chinese Medicine Syndrome

After treatment, the total effective rate of the experimental group was 95.8%, while that of the control group was 83.3%. The rank-sum test yielded Z=-2.092, P=0.036, indicating a statistically significant difference, as detailed in Table 10.

Table 10: Comparison of Efficacy of Traditional Chinese Medicine Syndrome Between the Two Groups (n, %)

Group	Clinical Cure/Cases (%)	Significant Effect/ Cases (%)	Effective/Cases (%)	Invalid/Cases (%)	Total Effective Rate (%)
Experimental Group (n=24)	0	5 (20.8%)	18 (75%)	1 (4.2%)	95.8%
Control Group (n=24)	0	1 (4.2%)	19 (79.2%)	4 (16.7%)	83.3%

Safety Indicators

Comparison of K+ Before and After Treatment in the Experimental Group

After treatment, there was no significant change in serum potassium levels in the experimental group ($P > 0.05$), and the difference was not statistically significant, as detailed in Table 11.

Table 11: Comparison of Serum Potassium in the Experimental Group [mmol/L, ±s/M(P25,P75)]

Group	Before Treatment	After Treatment	*t*	*z*	*P*
Experimental Group (n=24)	4.13(3.98,4.21)	4.23±0.34	-	-1.344	0.179

Comparison of ALT and AST Before and After Treatment in the Experimental Group

After treatment, there were no significant changes in ALT and AST levels in the experimental group ($P > 0.05$), and the differences were not statistically significant, as detailed in Tables 12 and 13.

Table 12: Comparison of ALT in the Experimental Group [U/L, M(P25,P75)]

Group	Before Treatment	After Treatment	*t*	*z*	*P*
Experimental Group (n=24)	21.5(17,35.75)	20(16.25,31)	-	-0.07	0.945

Safety Evaluation During Treatment in Both Groups

During the study treatment period, two patients in the experimental group experienced allergic reactions, manifested as rash and skin itching symptoms. The medication was promptly discontinued, and loratadine was administered for allergy treatment, resulting in a quick alleviation and disappearance of symptoms. No adverse drug reactions or other adverse events were reported in the control group, and no endpoint events occurred in either group.

Discussion

Proteinuria, as one of the important biomarkers for detecting the progression of glomerular diseases, is highly correlated with the degree of renal pathological damage. Clinical practice has confirmed that actively controlling proteinuria can not only delay disease progression but also achieve renal protective effects by reducing intraglomerular pressure and improving podocyte function. The data from this study show that in the longitudinal comparison within the group, the levels of 24-hour urinary protein (24hUpro) in both treatment groups were significantly lower after treatment compared to before treatment, with the experimental group showing a more significant effect in reducing proteinuria. This result corroborates the conclusions of previous clinical observations: the combination of traditional Chinese medicine or traditional Chinese medicine compound formulas with ARB medications can significantly enhance the efficacy of proteinuria control. The severity of hematuria is also significantly correlated with the prognosis of chronic glomerulonephritis (CGN). In recent years, Sevillano et al. found through multicenter cohort studies that persistent hematuria is an independent predictor of disease progression to end-stage renal disease (ESRD). The Bobart team further confirmed that the degree of microscopic hematuria is positively correlated with the glomerular filtration rate and is an independent predictor of renal function deterioration. The above evidence-based medicine demonstrates that effective control of hematuria is of great significance for improving the prognosis of CGN patients. The results of this study found that after treatment, the urinary red blood cell count (URBC) in both groups decreased compared to before, and the difference between the groups was statistically significant. This result suggests that the addition of the Qi-Zhi-Yi-Shen formula to the basic treatment has a synergistic effect in improving hematuria. This is consistent with previous research conclusions that traditional Chinese medicine compounds combined with ARB medications can effectively reduce urinary red blood cell excretion and protect renal function. In terms of renal function assessment, serum creatinine (Scr) concentration is an important indicator reflecting glomerular filtration function. The Scr levels in both groups decreased compared to baseline levels before treatment, with the experimental group showing a significantly greater reduction than the control group. This indicates that the Qi-Zhi-Yi-Shen formula has a significant advantage in improving renal function. Multiple randomized controlled trials have confirmed that the combination of traditional Chinese medicine compounds and ARB treatment provides better renal protection for CGN patients, and the results of this study further validate this conclusion. These data suggest that the Qi-Zhi-Yi-Shen formula may exert synergistic effects with ARB medications through various mechanisms such as regulating inflammatory responses and improving renal microcirculation, thereby effectively treating CGN and delaying disease progression [28-35].

Further statistical analysis showed that the overall clinical efficacy rate of the experimental group was 95.8%, significantly higher than the 83.3% of the control group, indicating better efficacy in the experimental group. This difference is attributed to the Qi-Zhi-Yi-Shen formula's multidimensional intervention in the pathological mechanisms of CGN, with its core mechanisms encompassing immune mechanisms, inflammatory reactions, oxidative stress, and renal fibrosis. Modern research indicates that the progression of CGN is essentially triggered by immune responses, which can activate inflammatory reactions and oxidative stress responses, thereby initiating fibrotic pathways. At the same time, inflammatory reactions and oxidative stress responses promote each other, ultimately leading to pathological damage such as proteinuria and renal fibrosis, resulting in progressive loss of renal function. The active components of Astragalus in the prescription can exert renal protective effects through various pathways, including inhibiting oxidative stress and inflammatory responses, and alleviating renal fibrosis. Hirudo, with its characteristic of "penetrating without hindrance," exerts anti-fibrotic and oxidative stress-inhibiting effects by downregulating the PI3K/AKT/mTOR signaling pathway, thereby inhibiting mesangial cell proliferation, maintaining podocyte stability, and ultimately reducing 24hUpro levels to protect renal function. Qingfeng Teng has multi-target anti-inflammatory, immunosuppressive, antioxidant, and microcirculation-improving effects. The traditional Chinese medicine Poria in the prescription can inhibit inflammatory responses and oxidative stress by downregulating the MCP-1/CCR2 signaling pathway, thereby alleviating renal injury in CGN rats. Puhuang has strong antioxidant activity, which can reduce IL-6 and TNF-α expression and inhibit inflammatory responses. Platycodon has been proven to possess various biological activities, including anti-inflammatory, antioxidant, anticoagulant, and anti-tumor effects. Epimedium can alleviate renal inflammatory responses by inhibiting the TLR4/NF-κB signaling pathway while significantly reducing 24hUpro and Scr levels, thus exerting renal protective effects. The Qi-Zhi-Yi-Shen formula can fully utilize the advantages of traditional Chinese medicine's multi-component and multi-target treatment, breaking through the limitations of traditional Western medicine's single-pathway inhibition, providing a new treatment paradigm for CGN [36-42].

In terms of improving traditional Chinese medicine syndromes, the syndrome scores of both groups of patients significantly decreased after treatment, with the experimental group showing more prominent effects. This result is consistent with findings from other previous studies. Further analysis showed that the total effective rate of the experimental group was 95.8%, while that of the control group was 83.3%. These data indicate that the Qi-Zhi-Yi-Shen formula has greater advantages in alleviating patients' discomfort symptoms and improving quality of life. From clinical experience, qi deficiency and blood stasis syndrome is the most common among outpatient patients, generally caused by long-term overwork depleting righteous qi, prolonged illness damaging the spleen and kidney, and aging leading to qi deficiency. This results in the decline of spleen and kidney function, qi deficiency, and subsequently an inability to promote blood circulation, leading to blood stasis and obstruction. If blood stasis obstructs the renal collaterals, it manifests as symptoms such as proteinuria and hematuria. This formula uses Astragalus as the main herb, taking advantage of its sweet and warm nature to greatly tonify the qi of the spleen and lung while promoting circulation; supplemented by Hirudo, which can deeply clear the hidden evil of stasis in the renal collaterals, adept at breaking blood and removing stasis, and unblocking collaterals; combined with Qingfeng Teng to dispel wind and eliminate dampness, unblocking collaterals. The three herbs work together to invigorate qi, activate blood, and unblock collaterals. At the same time, the prescription is adjusted in a timely manner according to changes in the patient's condition: adding Poria to strengthen the spleen, promote diuresis, and reduce edema; adding Puhuang charcoal to activate blood, resolve stasis, and stop bleeding to reduce hematuria; combining Platycodon and licorice to clear the lung, detoxify, and relieve throat pain; and adding Epimedium to warm the kidney and assist yang to alleviate the patient's cold intolerance symptoms. This fully reflects the advantages of traditional Chinese medicine's holistic concept and syndrome differentiation treatment [43].

There have been previous reports of cases related to drug-induced hyperkalemia and drug-induced liver injury caused by traditional Chinese medicine compounds and preparation. In addition, plant-based medicinal materials (especially whole herbs, flowers, and leaves) are rich in potassium, and potassium ions are more easily released after boiling due to their pharmacological properties. Moreover, some active components in traditional Chinese medicine, such as pyrrolidine alkaloids, can activate CYP450 enzymes to induce liver injury. Based on this, this study included serum potassium concentration and liver function indicators as safety indicators. The results showed that after treatment, the overall changes in blood potassium, alanine aminotransferase, and aspartate aminotransferase levels in the experimental group were not significant, and there was no statistical significance in the longitudinal comparison within the group. During clinical follow-up, two patients experienced allergic symptoms such as rash and skin itching, which disappeared after timely discontinuation of the medication and administration of loratadine for allergy. Subsequent follow-up showed no other discomfort in these patients. Literature review revealed previous reports of allergic reactions to the injection of Xuefu Zhuyu injection (main components being leeches and earthworms), with symptoms similar to those of the two patients in this study. However, since the number of individuals experiencing allergic symptoms was small relative to the total study population, it is inferred that the clinical application of Qi-Zhi-Yi-Shen formula is relatively safe [44-50].

There is no clear record of CGN disease name in ancient texts; it is generally classified according to clinical symptoms into categories such as "low back pain," "cloudy urine," and "hematuria," with the pathogenesis based on deficiency of righteous qi, dampness and turbidity, and blood stasis, which runs through all stages of disease occurrence and development [51].

The modern TCM theoretical system has reached a consensus that meridian disease is a basic pathological state widely present in various acute and chronic kidney disease processes. Tracing its origins, the "Huangdi Neijing" records that "when the disease is prolonged, the flow of nutrients and defenses becomes sluggish, and the meridians are occasionally unblocked," initially explaining the characteristics of meridians as being deficient due to loss of nourishment and solid due to stasis. In the Qing Dynasty, Ye Tianshi further proposed the transformation law of meridian disease, stating that "initially, qi is blocked in the meridians, and over time, blood injury enters the meridians," clarifying that the onset of meridian disease is a progressive process where pathogenic qi gradually enters the blood meridians. This is similar to the initial symptoms of CGN patients, which only manifest as fatigue and low back soreness, and later gradually develop into microscopic manifestations such as proteinuria and hematuria. Furthermore, from the perspective of pathogenesis, meridian disease is characterized by the ease of pathogenic factors entering but difficulty in exiting, qi and blood easily stagnating and stasis forming, and pathological products easily accumulating and taking shape. The mentor, combining years of experience in both Western and Chinese medicine, pointed out that the essence of CGN onset lies in congenital kidney qi deficiency and acquired spleen and stomach malnourishment, leading to qi deficiency unable to circulate blood, resulting in blood stasis obstructing the meridians. This evolution of pathogenesis aligns with the core mechanism of meridian disease, which is "deficiency and stasis intermingling." Additionally, research from a microscopic structural perspective reveals that components of the renal vascular system, such as glomerular capillary networks and glomerular arteries, have certain similarities in structure and function to what TCM refers to as kidney meridians. All of these reveal the connection between CGN and meridian disease theory [52-54].

Based on the above theoretical framework, the mentor emphasizes that the treatment of CGN should focus on combining tonifying deficiency and unblocking meridians, as both complement each other. The self-formulated Qi-Zhi-Yi-Shen formula consists of 40g of Astragalus, 10g of Hirudo, and 20g of Qingfeng Teng. The large dosage of Astragalus is used for its sweet and warm nature to tonify the deficiency of the five organs, while also regulating blood vessels and unblocking meridians, tonifying without stagnation, especially beneficial for invigorating qi and promoting water metabolism to address the root cause; Hirudo breaks blood stasis and promotes diuresis, utilizing its scavenging nature to clear the meridians; Qingfeng Teng is added to dispel wind, eliminate dampness, and promote diuresis, providing a pathway for the pathogenic factors to exit. If edema is present, Poria is added to strengthen the spleen and drain dampness, enhancing the diuretic effect in conjunction with Astragalus; if hematuria is observed, Puhuang charcoal is added to both resolve stasis and enhance hemostatic effects; if accompanied by sore throat or tonsillar suppuration, Platycodon is added to clear the lungs and benefit the throat, combined with Licorice for detoxification and throat relief, together forming the meaning of Ganju Decoction; if there is significant cold intolerance due to yang deficiency, Epimedium is added to warm the kidney and assist yang, while also dispelling wind and dampness. The entire formula integrates methods of tonifying and activating blood, allowing the spleen qi to function properly to control water, the kidney qi to be replenished to govern water, and the stasis to be removed for smooth meridian flow, achieving simultaneous treatment of both symptoms and root causes, thus reinforcing healthy qi and dispelling pathogenic factors.

Conclusion

The application of Qi-Zhi-Yi-Shen formula on the basis of conventional Western medicine treatment can significantly improve the TCM syndrome scores, kidney function indicators, urine protein quantification, and urine red blood cell count in patients with chronic glomerulonephritis, with good safety.

References

1. Wang J, Zhou C, Lu L, Shoujun Wang, Qing Zhang, et al. (2024) Differentiated metabolomic profiling reveals plasma amino acid signatures for primary glomerular disease [J]. Amino Acids 56: 46.
2. Yang C, Wang H, Zhao X, Kunihiro Matsushita, Josef Coresh, et al. (2020) CKD in China: Evolving Spectrum and Public Health Implications [J]. Am J Kidney Dis 76: 258-264.
3. Gui Ke, Zhang Qiulin, Xu Jinrong (2024) Research Progress on the Combined Treatment of Chronic Glomerulonephritis with Chinese and Western Medicine [J]. Health Medicine Research and Practice 21: 144-148.
4. Kronbichler A, Bajema I, Geetha D, Saemann M (2023) Novel aspects in the pathophysiology and diagnosis of glomerular diseases [J]. Ann Rheum Dis 82: 585-93.
5. Shi Zhaoyu, Wang Xinquan, Gu Hongmei, et al. (2021) Application of Native T1-mapping in Assessing Renal Fibrosis in Chronic Glomerulonephritis [J]. Chinese Journal of Medical Imaging 29: 930-934.
6. Ren Jing, Deng Deqiang (2021) Research Progress on Chronic Glomerulonephritis in Chinese and Western Medicine [J]. Xinjiang Journal of Traditional Chinese Medicine and

Pharmacy 39: 113-116.

7. Mei Mei, Zhang Qian, Shen Bingbing (2020) Application Value of Dual Renin-Angiotensin System Inhibition Strategy in Cardiovascular Diseases [J]. Journal of Clinical and Pathology 40: 3000-3005.
8. Gan Liangying, Zuo Li, Xiaoxi Lyu, Xiangdong Yang, Zhanzheng Zhao, et al. (2023) Expert Group on the Application of Angiotensin Receptor-Endopeptidase Inhibitors in Chronic Kidney Disease Patients,. Chinese Expert Consensus on the Application of Angiotensin Receptor-Endopeptidase Inhibitors in Chronic Kidney Disease Patients [J]. Chinese Journal of Blood Purification 22: 241-253.
9. Kidney Disease: Improving Global Outcomes Glomerular Diseases Work G. Kdigo (2021) Clinical Practice Guideline for the Management of Glomerular Diseases [J]. Kidney Int 100: S1-S276.
10. Esteras R, Perez-Gomez M V, Rodriguez-Osorio L, Alberto OrtizBeatriz Fernandez-Fernandez (2015) Combination use of medicines from two classes of renin-angiotensin system blocking agents: Risk of Hyperkalemia, Hypotension, and Impaired Renal Function [J]. Ther Adv Drug Saf 6: 166-176.
11. Wu Jian, Fu Tongfei, Yuan Jun (2024) Meta-analysis of Bailing Capsules Combined with ACEI/ARB in the Treatment of Chronic Glomerulonephritis [J]. Western Journal of Traditional Chinese Medicine 37: 60-64.
12. He Yangmiao, Liao Shuheng, Sun Shangping (2024) Discussion on the Formulation Rules of Invigorating Spleen and Replenishing Qi, Clearing Heat and Draining Dampness in the Treatment of Chronic Glomerulonephritis Based on the Inheritance Computing Platform of Traditional Chinese Medicine [J]. Jiangxi Journal of Traditional Chinese Medicine and Pharmacy 55: 46-49.
13. Yang Yazhen, Zhou Liusha (2022) Discussion on Professor Wang Yongjun's Treatment Ideas for Kidney Wind Disease Based on Medical Case Deconstruction [J]. Journal of Zhejiang University of Traditional Chinese Medicine 46: 969-973.
14. Feng M, Lv J, Zhang C, Dagui Chen, Huan Guo, et al. (2022) Astragaloside IV Protects Sepsis-induced Acute Kidney Injury by Attenuating Mitochondrial Dysfunction and Apoptosis in Renal Tubular Epithelial Cells [J]. Curr Pharm Des 28: 2825-2834.
15. Tang L, Zhu M, Che X, Xiaoqian Yang, Yao Xu ,et al. (2022) Astragaloside IV Targets Macrophages to Alleviate Renal Ischemia-Reperfusion Injury via the Crosstalk between Hif-1alpha and NF-kappaB (p65)/Smad7 Pathways [J]. J Pers Med 13: 59.
16. Feng H, Zhu X, Tang Y, Shouqiang Fu, Bingtan Kong, et al. (2021) Astragaloside IV Ameliorates Diabetic Nephropathy in Db/Db Mice by Inhibiting Nlrp3 Inflammasome Mediated Inflammation [J]. Int J Mol Med 48.
17. Junren C, Xiaofang X, Huiqiong Z, Li Gangmin, Yin Yanpeng, et al. (2021) Pharmacological Activities and Mechanisms of Hirudin and Its Derivatives - A Review [J]. Front Pharmacol 12: 660757.
18. Guo Xiaona, Zhang Nan, Niu Meilan (2024) Effect of Hirudin on Glucose Metabolism Levels and Renal Function Protection in Diabetic Nephropathy Rats [J]. Chinese Journal of Gerontology 44: 4297-4301.
19. Wang W, Cai J, Tang S, Ying Zhang, Xuejing Gao, et al. (2016) Sinomenine Attenuates Angiotensin II-Induced Autophagy via Inhibition of P47-Phox Translocation to the Membrane and Influences Reactive Oxygen Species Generation in Podocytes [J]. Kidney Blood Press Res 41: 158-167.
20. Jiang Yihong, Zheng Jiaxin (2023) GEO Chip Analysis Combined with Network Pharmacology to Explore the Mechanism of Qingfeng Teng in Treating Idiopathic Membranous Nephropathy [J]. Health Research 43: 672-677.
21. Xie Yuduan, Li Hanlian, Han Yan (2025) Effect of Poria Acid on MCP-1/CCR2 Signaling Pathway in Inflammatory Response of Rats with Chronic Glomerulonephritis [J]. Modern Immunology 45: 37-42.
22. Wang Wanting, Xu Ying, Shao Minghai (2023) Research Progress on Chinese Medicinal Monomers Targeting PI3K/Akt/mTOR Signaling Pathway in Preventing and Treating Diabetic Kidney Disease [J]. Shanghai Journal of Traditional Chinese Medicine 57: 83-88.
23. Chen Yan, Li Ying, Yang Qiong (2024) Research Progress on the Biological Activity and Application of Glycyrrhetinic Acid [J]. Chinese Herbal Medicine 55: 7507-7518.
24. Chen Xingxing, Lü Dongning, Li Yingrui, Liu Mingmin (2024) Research Progress on TCM Pairs in the Treatment of Chronic Kidney Disease [J]. Clinical Research of Traditional Chinese Medicine 16: 68-72.
25. Yuan Ling, Wang Lei, Wang Hong (2024) Icariin Regulates TGF-β1 Induced DNA Hyper-Methylation to Inhibit Proliferation of Renal Interstitial Myofibroblasts in 5/6 Nephrectomized Rats [J]. Drug Evaluation Research 47: 2770-2777.
26. Ge Junbo, Wang Chen, Wang Jianan (2024) Internal Medicine. 10th Edition [M]. Internal Medicine. 10th Edition.
27. XY Zheng, X. Zheng, X Zheng (2002) Guidelines for Clinical Research of New Traditional Chinese Medicines: Trial Implementation [J]. China Medical Science and Technology Press https://www.scienceopen.com/book?vid=61e80b22-e0f0-442d-aba3-bbc692b48bd7.
28. Murton M, Goff-Leggett D, Bobrowska A, Juan Jose Garcia Sanchez , Eric Wittbrodt, et al. (2021) Burden of Chronic Kidney Disease by KDIGO Categories of Glomerular Filtration Rate and Albuminuria: A Systematic Review [J]. Adv Ther, 38: 180-200.
29. Yu Jianjun, Yuan Wenjing, Shi Xuhui, Qin Yang (2025) The Effect of Huang Kui Capsules Combined with Irbesartan on Patients with Chronic Glomerulonephritis [J]. Chinese Journal of Min-Kang Medicine 37: 85-88.
30. Sevillano AM, Gutierrez E, Yuste C, Teresa Cavero, Evangelina Mérida, et al. (2017) Remission of Hematuria Improves Renal Survival in IgA Nephropathy [J]. J Am Soc Nephrol 28: 3089-3099.
31. Bobart SA, Alexander MP, Shawwa K, Lisa E Vaughan, Sanjeev Sethi, et al. (2021) The association of microhematuria with mesangial hypercellularity, endocapillary hypercellularity, crescent score and renal outcomes in immunoglobulin A nephropathy [J]. Nephrol Dial Transplant 36: 840-847.
32. Xie Xiaodong, Li Xiaosheng (2021) Clinical observation of integrated traditional Chinese and Western medicine in the treatment of chronic glomerulonephritis [J]. Chinese Modern Distance Education of Traditional Chinese Medicine 19: 127-129.
33. Levey AS, Perrone RD, Madias NE (1988) Serum creatinine and renal function [J]. Annu Rev Med 39: 465-490.
34. Lü Sujuan (2023) Analysis of the Effect of Jianpi Yiqi Qingli Huayu Decoction Combined with Irbesartan on Proteinuria Levels in Chronic Nephritis [J]. Northern Pharmacy 20: 12-14.
35. Hu Zhuangbin (2022) Observation Of the Effect of Huang Kui Capsules Combined with Irbesartan in the Treatment of Chronic Glomerulonephritis [J]. Chinese Modern Drug

Application 16: 100-102.
36. Xue HZ, Chen Y, Wang SD, Yi-Meng Yang, Lu-Qi Cai, et al. (2024) Radix Astragali and Its Representative Extracts for Diabetic Nephropathy: Efficacy and Molecular Mechanism. J Diabetes Res [J] 14: 5216113.
37. Ma Hailan, Ma Hongbin, Li Xuping (2025) Research Progress on Effective Components of Hirudo and Pheretima in Preventing and Treating Renal Fibrosis [J]. Journal of Clinical Traditional Chinese Medicine 37: 187-193.
38. Liu Jun Guang, Feng Zhi Li, Li Meng, (2024) The Effects of Active Components of Qingfeng Teng on Oxidative Stress, Inflammatory Response, and Immune Function in Diabetic Db/Db Mice [J]. Hebei Journal of Traditional Chinese Medicine 39: 1-7.
39. Teng Jian, Zhao Lijuan, Zhou Sihang (2019) Research progress on the treatment of kidney disease with hydrochloride of Qing Teng alkaloid [J]. Journal of Traditional Chinese Medicine 25: 120-124.
40. Chen T, Chen C, Huang Y, Rathinasamy Baskaran, Jeffrey J P Tsai, et al. (2021) Ethanolic extract of Puhuang (Pollen Typhae) modulates lipopolysaccharide-induced inflammatory response through inducible nitric oxide synthase / cyclooxygenase-2 signaling in RAW 264.7 macrophage [J]. J Tradit Chin Med 41: 836-844.
41. Ge FL, Niu M, Han ZX, Yan-Fang Zhang, Jia-Bo Wang et al. (2019) Analysis of Epidemiological Characteristics of Drug Induced Liver Injury Associated with Baixianpi Preparations] [J] 44: 1048-1052.
42. Wang Yuhui, Lou Zhengqing, Chen Xiaofan (2004) Analysis of Potassium Content in Commonly Used Traditional Chinese Medicine Decoctions [j]. Chinese Journal of Integrated Traditional and Western Medicine Nephrology 5: 531-532.
43. Chen Qingshu, Wang Xiaohui, Wang Daimei, Wang Yingyan (2019) Pharmaceutical analysis of hyperkalemia caused by traditional Chinese medicine [J]. Chinese Journal of Traditional Chinese Medicine Information 26: 133-135.
44. Ma J, Li M, Li N, Wood Yee Chan, Ge Lin (2021) Pyrrolizidine Alkaloid-Induced Hepatotoxicity Associated with the Formation of Reactive Metabolite-Derived Pyrrole-Protein Adducts [J]. Toxins (Basel) 13: 723.
45. Liu Fenghua (2016) Treatment and Nursing of an Allergic Reaction to Shuxuetong Injection [j]. World Latest Medical Information Abstracts 16: 219.
46. Meng Chunping, Wang Zhiwei (2020) The Effect of Jianpi Quyu Huoxue Decoction as an Adjunctive Treatment for Chronic Glomerulonephritis on Serum Inflammatory Factors and Cellular Immune Function [J]. Chinese Journal of Preventive Medicine 21: 262-266.
47. Meng Yuan, Wang Yu, Zhao Wenjing (2022) Gao Yanbin's Experience in Treating Adult Iga Vasculitis-Related Nephritis from the Perspective of Meridian Disease [J]. Beijing Traditional Chinese Medicine 41: 746-750.
48. Li Hongrong, Wu Yiling (2021) Inheritance and innovation of meridian disease research 41: 836-844.
49. Xie L, Zhao Y X, Zheng Y, Li X F (2023) The Pharmacology and Mechanisms of Platycodin D, an Active Triterpenoid Saponin from Platycodon Grandiflorus [J]. Front Pharmacol 14: 1148853.
50. Qi MY, He Y H, Cheng Y, Qing Fang, Ru-yu Ma, et al. (2021) Icariin Ameliorates Streptozocin-Induced Diabetic Nephropathy Through Suppressing the Tlr4/Nf-Kappab Signal Pathway [J]. Food Funct 12: 1241-1251.
51. Xiong Yuanyuan, Li Sha, Mo Yihao, Liu Jiadong (2023) The Efficacy of Jianpi Quyu Huoxue Decoction Combined with Losartan in Treating Qi Deficiency and Blood Stasis Type Chronic Glomerulonephritis and Its Effects on Serum cys-c, α1-mg levels, and lymphocyte subsets [j]. Sichuan Traditional Chinese Medicine 41: 136-140.
52. Liang Huan, Zheng Tao, Xie Zhao (2024) Pharmaceutical Monitoring of a Suspected Case of Acute Hyperkalemia in a Patient with Ckd Stage 5 Caused by Traditional Chinese Medicine [J]. Chinese Pharmacist 27: 177-180.
53. Gu Yifei, Dou Dani (2020) A Case of Hyperkalemia Caused by Traditional Chinese Medicine Stone-Removing Granules [J]. Chinese Modern Applied Pharmacy 37: 2277-2278.
54. TANG Lingling, ZHAO Xia, YAN Hua , WU Jiabao (2022) Journal of Nanjing University of Traditional Chinese Medicine 38: 1075-1085.
55. Cao fang, wen kejian, gao leiping, wang yue (2024) Discussion on the Correlation between "kidney Deficiency and Blood Stasis" Pathogenesis Based on Collateral Disease Theory and Insufficient Autophagy in Elderly Chronic kidney Disease [J]. Journal of Traditional Chinese Medicine and Pharmacy 36: 1647-1650.

Copyright: ©2025 Dapeng Wang, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.