

Artículo Original / Original Article

Retrospective analysis of the clinical efficacy of BuzhongQingli decoction in immunoglobulin A nephropathy exhibiting the dampness-heat due to spleen deficiency syndrome

[Análisis retrospectivo de la eficacia clínica de la decocción BuzhongQingli en la nefropatía por inmunoglobulina A que presenta el síndrome de humedad-calor debido a deficiencia del bazo]

Jing Tao¹, Zhi-Lin Zhang², Ran Liu¹, Xiao-Ning Tan¹, Hao Li³, Li-Ming Zhao¹, Yu-Rong Cheng¹ & Da-Jun Yu³

¹Graduate School, China Academy of Chinese Medical Sciences, Beijing, China

²Graduate School, Shanxi University of Chinese Medicine, Jinzhong, Shanxi Province, China

³Renal Unit, Xiyuan Hospital, China Academy of Chinese Medical Sciences, Beijing, China

Reviewed by:

Wenju Gu
Universidad de Antioquia
Colombia

Francisco J. Jimenez
Universidad Tecnológica de Pereira
Colombia

Correspondence:

Da-Jun YU
dajunyudj@126.com

Section Clinical Activity

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Abstract: To investigate the effect of BuzhongQingli Decoction (BZQLT) on the symptoms, hematuria, proteinuria, serum creatinine (SCr) of patients with immunoglobulin A nephropathy (IgAN), exhibiting the dampness-heat due to spleen deficiency syndrome. Methods: Patients with IgAN who were treated with BZQLD over a three-month period between 2022 and 2023, were enrolled in this study. Data collected included TCM syndrome scores, urine red blood cell count/HP, 24-hour urinary protein quantification (24-UTP), SCr before and after treatment. Results: Treatment with BZQLD over three months led to significant reductions in TCM syndrome scores, urine red blood cell count/HP, 24-UTP, and SCr levels in 62 patients. Conclusion: BZQLD effectively reduces the TCM syndrome scores and improves key clinical efficacy indicators in patients with IgAN presenting with the dampness-heat due to spleen deficiency syndrome, demonstrating its substantial clinical efficacy.

Keywords: BuzhongQingli Decoction; Clinical efficacy; Dampness-heat due to spleen deficiency syndrome; IgA nephropathy; Retrospective study.

Resumen: Este estudio tiene como objetivo investigar el efecto de la decocción BuzhongQingli (BZQLT) sobre los síntomas, hematuria, proteinuria y creatinina sérica (SCr) en pacientes con nefropatía por inmunoglobulina A (IgAN), que presentan el síndrome de humedad-calor debido a deficiencia del bazo. Métodos: Se incluyeron en este estudio pacientes con IgAN que fueron tratados con BZQLD durante un período de tres meses entre 2022 y 2023. Los datos recopilados incluyeron puntuaciones del síndrome de medicina tradicional china (MTC), recuento de glóbulos rojos en orina/HP, cuantificación de proteína urinaria de 24 horas (24-UTP) y SCr antes y después del tratamiento. Resultados: El tratamiento con BZQLD durante tres meses condujo a reducciones significativas en las puntuaciones del síndrome MTC, recuento de glóbulos rojos en orina/HP, 24-UTP y niveles de SCr en 62 pacientes. Conclusión: BZQLD reduce efectivamente las puntuaciones del síndrome MTC y mejora los indicadores clave de eficacia clínica en pacientes con IgAN que presentan el síndrome de humedad-calor debido a deficiencia del bazo, demostrando su sustancial eficacia clínica.

Palabras clave: Decocción BuzhongQingli; Eficacia clínica; Síndrome de humedad-calor debido a deficiencia del bazo; Nefropatía por IgA; Estudio retrospectivo.

INTRODUCTION

Immunoglobulin A nephropathy (IgAN), recognized as the most prevalent primary glomerulonephritis worldwide, leads to end-stage renal disease (ESRD) in approximately 20% to 40% of cases within two to three decades of diagnosis (Selvaskandan *et al.*, 2022), rendering IgAN a principal contributor to ESRD (Pitcher *et al.*, 2023). Patients presenting with mild IgAN may experience asymptomatic gross hematuria, and those with advanced disease may experience massive hematuria (gross/microscopic) associated with varying degrees of proteinuria, often superimposed with respiratory or gastrointestinal infections as the disease rapidly progresses (Floege & Feehally, 2016). Currently, the pathogenesis of IgAN remains elusive, and Western medicine lacks specific pharmacological treatments, relying primarily on symptomatic management supplemented by glucocorticoids and immunosuppressants, which are associated with notable side effects (Rauen *et al.*, 2015; Lv *et al.*, 2017).

In contrast, traditional Chinese medicine (TCM) has gained recognition for its unique approach and benefits in treating IgAN. For instance, a cohort study by Wang *et al.* (2017), demonstrated that a double-dose of tripterygium glycosides (120 mg/d) as induction therapy significantly elevated the remission rate in IgAN without concomitant escalation in adverse events; similarly Kunxian capsule exhibited safety and efficacy in the treatment of IgAN (Le *et al.*, 2022).

Drawing from his extensive clinical experience, Professor Yu Dajun developed the "BuzhongQingli Decoction (BZQLD)" for treating IgAN characterized by the dampness-heat due to spleen deficiency syndrome. This formulation has demonstrated significant efficacy in alleviating the symptoms of discomfort in patients and improving clinical indicators, thereby significantly preserving renal function, and impeding disease progression. However, the absence of extensive research data undermines definitive validation of its efficacy. The aim of this study is to investigate the clinical efficacy of BZQLD in the treatment of IgAN exhibiting the dampness-heat due to spleen deficiency syndrome. We assessed the changes in hematuria, proteinuria, renal function and other indicators pre- and post-treatment with BZQLD in patients with IgAN manifesting the dampness-heat due to spleen deficiency syndrome and verified the efficacy of this

formulation.

MATERIALS AND METHODS

Criteria for diagnosis

Western medicine diagnostic criteria

(1) The pathological diagnosis of renal biopsy served as the standard, wherein the presence of IgA or IgA-based immunoglobulins along with complement C3 deposition in a granular pattern within the glomerular mesangial area or capillary wall were identified under immunofluorescence.

(2) Other secondary IgAN, such as Henoch-Schonlein purpura nephritis, hepatitis B-related nephritis, and lupus nephritis, were systematically excluded.

TCM syndrome type diagnostic criteria

The TCM syndrome differentiation criteria for the dampness-heat due to spleen-deficiency syndrome, as delineated in the TCM syndrome differentiation scheme of the National IgA Nephropathy Collaborative Center and the Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine in the Treatment of Chronic Nephritis, were utilized for syndrome differentiation and scoring.

Diagnostic criteria for the dampness-heat due to spleen deficiency syndrome included the following main symptoms: ① Low spirit and fatigue; ② decreased appetite; ③ abdominal distension after eating; and ④ loose stools. Additional minor symptoms comprised of: ① Lusterless facial complexion; ② bitter taste; ③ edema; ④ thin, soft-thin or soft-rapid of pulse; and ④ thin yellow or yellow coating on the tongue. Diagnosis was confirmed when two primary and two secondary symptoms were clinically observed.

Inclusion and exclusion criteria

- (1) Confirmation of IgAN through renal biopsy pathology.
- (2) Age ranging from 18 to 70 years.
- (3) Administration of BuzhongQingli Decoction as the primary therapeutic agent, with modifications as necessary.
- (4) Chronic kidney disease (CKD) classified within stages 1 to 3, characterized by an estimated glomerular filtration rate (eGFR) of 30 ml/min/1.73m² or higher.
- (5) Traditional Chinese medicine syndrome differentiation conforms to spleen deficiency

- and damp heat syndrome;
- (6) Complete clinical data, such as traditional Chinese medicine diagnosis information, laboratory test reports, pathological reports, etc;
 - (7) The continuous diagnosis and treatment time is 3 months;
 - (8) 24-hour urinary protein quantification <2.5g/24 h

Exclusion Criteria

- (1) Presence of secondary IgAN factors, including Henoch-Schonlein purpura nephritis, systemic lupus erythematosus, and liver disease-related factors.
- (2) Severe concurrent conditions such as serious infections or malignant hypertension, which could exacerbate the primary disease.
- (3) Incomplete clinical data which precludes comprehensive assessment and follow-up.
- (4) Poor patient compliance or inconsistent follow-up that could interfere with study results.
- (5) Restriction from using patient's previous medical records for scientific research due to existing stipulations.

Study methods

A retrospective study was conducted to identify individuals pathologically diagnosed with IgAN through renal biopsy at the Nephrology Department of Xiyuan Hospital, China Academy of Chinese Medical Sciences between January 2022 and December 2023. Patient data including body mass index (BMI), TCM syndrome manifestations and laboratory parameters such as urine red blood cell count/HP, 24-hour urine protein quantification, serum creatinine (SCr), eGFR, liver function, and blood routine analyses were collected utilizing the Haitai Outpatient Electronic Medical Record System, Ruimei Laboratory System, and Outpatient Medical Record Manual of Xiyuan Hospital, and China Academy of Chinese Medical Sciences.

Treatment Regimens

(1) Basic treatment: ① Lifestyle modifications: strict adherence to a low sodium diet (< 5 g/day), appropriate protein intake (0.8 g/kg/day), smoking cessation, appropriate exercise, blood pressure control less than 130/80 mmHg. Patients presenting with hyperlipidemia were administered atorvastatin calcium tablets, and those with hyperuricaemia were

administered febuxostat tablets. Glucocorticoid, immunosuppressive agents, and tripterygium glycosides tablets were contraindicated during the study period. ② Drug treatment: For patients exhibiting urinary protein quantification exceeding 0.5 g/day, ACEI or ARB drugs were prescribed at the maximum dose tolerated by the body.

(2) TCM treatment: All patients were administered the BZQLD. The duration of treatment was 3 months, with one dose administered daily, prepared as a decoction in water. The composition of the BZQLD is as follows: *Codonopsis pilosula* (10-15 g), Raw *Astragalus membranaceus* (10-15 g), *Poria cocos* (10-15 g), *Scutellaria baicalensis* (10-15g), Foochow yam rhizome (10 g), Coix seed (30 g), Fried *Atractylodes macrocephala* (10-15 g), Fried stiff silkworm (10 g), and Dioscoreae Spongiosae Rhizoma (15-20 g).

Outcome measures

Clinical efficacy of Chinese and Western medicine TCM syndrome scores

In alignment with the syndrome differentiation standards for spleen deficiency and dampness-heat syndrome, as established by the National IgA Nephropathy Collaborative Center, and in accordance with the "Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine in the Treatment of Chronic Nephritis", the TCM syndromes in patients were differentiated. The TCM syndrome scores were documented both before and after three months of treatment.

Scoring criteria: The primary symptoms were scored 2, 4, and 6 points based on their severity, including manifestations such as lack of spirit and fatigue, decreased appetite, abdominal distension after eating, loose stools, hematuria, and foamy urine.

The secondary symptoms were scored 1, 2, and 3 points based on their severity, primarily including manifestations such as lusterless facial complexion, bitter taste, and edema.

Additionally, patients meeting diagnostic criteria based on tongue and pulse examination were scored 1 point and while those not meeting these criteria were scored 0 points.

TCM syndrome efficacy

The efficacy evaluation of TCM syndromes was performed with reference to the Guidelines for

Clinical Research of New Drugs of Traditional Chinese Medicine in 2002, as shown in Table No. 1.

Laboratory parameters

The primary efficacy indicators of urine red blood cell count/HP (RBC/HP), 24-hour urinary protein quantification (24-UTP), SCr, eGFR (CKD-EPI

formula), secondary efficacy indicators of blood uric acid (UA), plasma albumin (ALB), hemoglobin (HGB), cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and safety indicators of liver function (ALT, AST), and HGB were systematically recorded for evaluation.

Table No. 1
TCM syndrome efficacy evaluation table

Efficacy determination	Symptom description	Syndrome scores
Complete remission	TCM clinical symptoms and signs disappeared or basically disappeared	≥ 95% decrease
Significant effectiveness	TCM clinical symptoms and signs significantly improved	≥ 70% decrease
Moderate effectiveness	TCM clinical symptoms and signs improved	≥ 30% decrease
No effect	None of the signs improved or some even worsened	< 30% decrease

Note: The calculation formula (nimodipine method) is [(score before treatment - score after treatment) ÷ score before treatment] × 100%; TCM: traditional Chinese medicine

Clinical efficacy

According to "Diagnosis, Syndrome Differentiation and Efficacy Evaluation of IgA Nephropathy" and "Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine":

Complete remission: clinical symptoms completely disappeared, urine sediment microscopy showed red blood cell count ≤ 3/HP, 24-hour urine protein quantification ≤ 0.3 g, and normal or stable renal function at the baseline level.

Significant effectiveness: denoted by substantial disappearance of clinical symptoms, the count of red blood cells in urine sediment microscopy decreased by ≥ 50%, the 24-hour urine protein quantification decreased by ≥ 50%, and the renal function was normal or stable at the baseline level.

Moderate effectiveness: manifested by significant improvement in clinical symptoms, the count of red blood cells in urine sediment microscopy was reduced by ≥ 25% and < 50% in comparison with the initial values, the 24-hour urinary protein quantification was reduced by ≥ 25% and < 50% in comparison with the initial values. The renal function was normal or stable at the baseline level.

No effect: characterized by the absence of improvement or exacerbation of clinical manifestations and laboratory tests results.

Primary Endpoint Events

Primary endpoint events were defined as either a

doubling of SCr post-treatment in comparison to pre-treatment levels or eGFR falling below 15 mL/min.

Statistical methods and analysis

Statistical analyses were carried out using SPSS version 26.0. Initially, normality tests were conducted to determine the distribution of the data. For data adhering to a normal distribution, results were presented as mean ± standard deviation and analyzed using the paired sample t-test. For data that did not follow a normal distribution, results were expressed as the median and interquartile range (P25, P75) and analyzed using non-parametric rank sum tests. A significance threshold was set at $p < 0.05$ to determine statistical significance.

Study Results

General information

In this study, a cohort of 62 patients diagnosed with IgAN and presenting with the dampness-heat due to spleen deficiency syndrome were included. Among these patients, 25 were males (40.3%) and 37 were females (59.7%), resulting in a male-to-female ratio of 1:1.48. Age distribution was as follows: 1 patient (1.6%) aged 18–19 years, 14 patients (22.58%) aged 20–29 years, 18 patients (29.03%) aged 30–39 years, 16 patients (25.81%) aged 40–49 years, 7 patients (11.29%) aged 50–59 years, and 6 patients (9.68%) aged 60–70 years, as shown in Figure No. 1. The average age was 38.48 ± 10.18 years in males and

40.59 ± 14.06 years in females. The BMI of the cohort ranged from 17.2 and 32.8, with a mean BMI of 23.12 ± 3.10. Thirty-seven patients (59.68%) had a history of hypertension, 32 patients (51.61%) had a history of hyperlipidemia, and 36 patients (58.06%)

had a history of hyperuricaemia. Twenty-eight patients (45.16%) were in stage 1 of chronic kidney disease (CKD), 18 patients (29.03%) were in stage 2 of CKD, and 16 patients (25.81%) were in stage 3 of CKD.

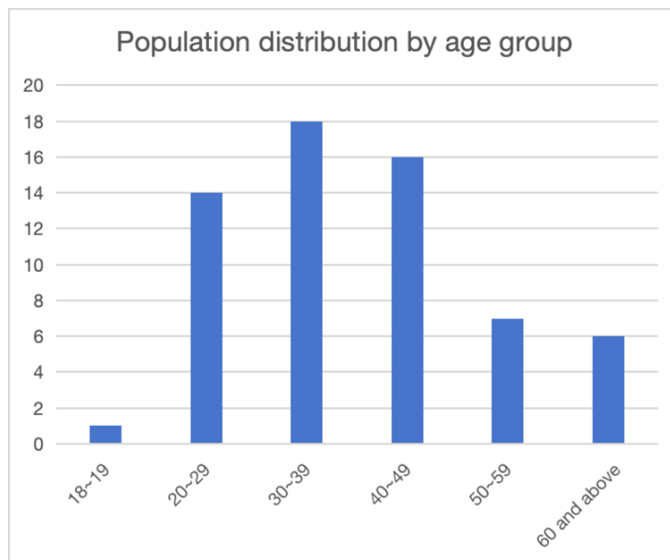


Figure No. 1
Age distribution of patients

Comparison of TCM and Western medicine efficacy **Comparison of TCM syndrome scores**

The patients enrolled in this study presented a TCM syndrome score of 16.03 ± 5.02 before treatment and 9.42 ± 3.54 after treatment. This observed difference was statistically significant ($p < 0.01$).

Evaluation of TCM syndrome efficacy

Among the study participants, 4 patients (6.45%) achieved complete remission, 22 patients (35.48%) experienced significant effectiveness, 30 patients (48.39%) experienced moderate effectiveness, 6 patients (9.68%) reported no effect. The overall response rate was calculated at 90.32%, as shown in Figure No. 2.

Clinical Efficacy Evaluation

Among the study participants 5 patients (8.06%) achieved complete remission, 19 cases (30.65%)

experienced significant effectiveness, 28 patients (45.16%) experienced moderate effectiveness and 10 patients (16.13%) reported no effect. The overall response rate was calculated at 83.87%, as shown in Figure No. 3.

Laboratory parameters

Primary Efficacy Measures

A comparative analysis was conducted on the principal efficacy indicators both before and after treatment. It was observed that urine red blood cell count/HP, 24-hour urinary total protein (24-UTP), SCr, and eGFR conformed to a normal distribution pattern. Paired sample t-test was used for statistical analysis. There was a significant reduction in urine red blood cell count/HP, 24-UTP, and SCr and an increase in eGFR at the end of the follow-up phase, and the differences were statistically significant ($p < 0.05$), as shown in Table No. 2.

Table No. 2
Primary Efficacy Measures

	Pre-treatment	At the end of follow-up	t	P
Urine red blood cell count (HP)	27.43 ± 24.95	9.97 ± 11.97	6.835	<i>p</i> <0.01
Urinary protein quantification (g/24h)	0.97 ± 0.81	0.62 ± 0.62	4.135	<i>p</i> <0.01
Blood creatinine (μmol/L)	93.26 ± 40.07	87.33 ± 35.85	5.645	<i>p</i> <0.01
Glomerular filtration rate (mL/min/1.73 m ²)	84.32 ± 30.64	88.50 ± 29.17	-4.311	<i>p</i> <0.01

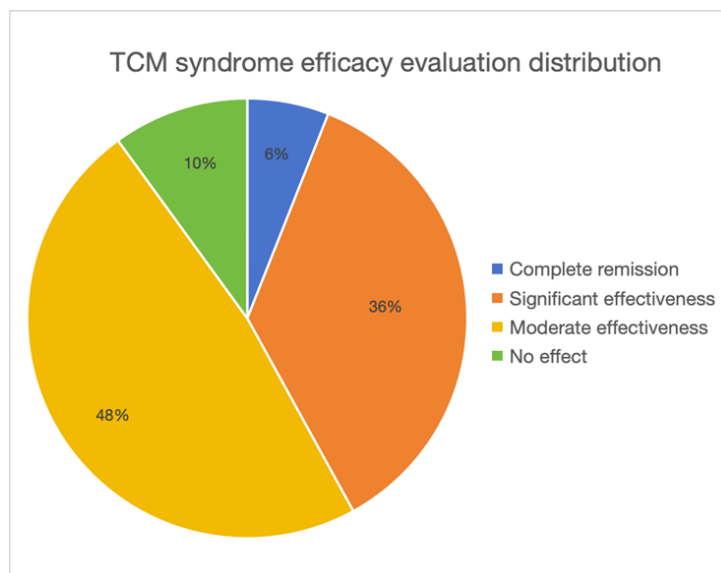


Figure No. 2
TCM syndrome efficacy evaluation distribution

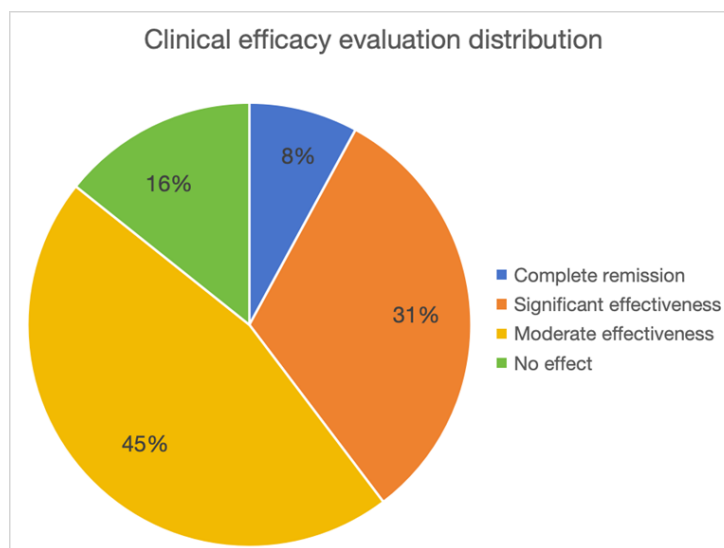


Figure No. 3
Clinical efficacy evaluation distribution

Secondary Efficacy Measures

Parameters like UA, TC, TG, HDL, LDL and ALB exhibited a skewed distribution and were subjected to paired sample rank sum test. The results showed that there was no statistical difference in UA, TC, TG, HDL, LDL and ALB ($p>0.05$), as shown in Table No. 3.

Safety Measures Comparison

There was no significant difference in liver function (ALT, AST) and blood routine (HGB) before and after treatment ($p>0.05$), and no incidence of adverse events, as shown in Table No. 4.

Table No. 3
Secondary efficacy indicators

Indicators	Pre-treatment	At the end of follow-up	Z	p
Blood uric acid ($\mu\text{mol/L}$)	339 (280.75, 399)	337 (299.75, 398.25)	-0.649	0.517
Total cholesterol (mmol/L)	5.57 (3.82, 5.38)	4.33 (3.72, 5.32)	-0.661	0.509
Triglyceride (mmol/L)	1.23 (0.99, 1.98)	1.34 (1.05, 1.73)	-1.103	0.27
High density lipoprotein (mmol/L)	1.29 (1.11, 1.535)	1.36 (1.1, 1.54)	-1.43	0.153
Low-density lipoprotein (mmol/L)	2.42 (1.72, 3.02)	2.46 (1.93, 2.99)	-0.83	0.407
Plasma albumin (g/L)	42.19 (40.28, 44.59)	42.66 (40.32, 44.51)	-0.308	0.758

Table No. 4
Changes in safety indicators

Indicators	Pre-treatment	At the end of follow-up	Z	P
Alanine aminotransferase (U/L)	14 (9.3, 20.68)	14.5 (9.58, 25.7)	-1.373	0.170
Aspartate aminotransferase (U/L)	16.6 (14, 19.5)	17.55 (14.6, 21.75)	-1.473	0.141
Hemoglobin (g/L)	138 (122.75, 148.75)	136.5 (123.5, 147)	-1.128	0.259

Primary Endpoint Events

There was no doubling of SCr or eGFR less than 15 mL/min/1.73 m² during the follow-up period, thus indicating the absence of primary endpoint events.

DISCUSSION

IgAN exhibits a high prevalence in China, with diagnosis primarily reliant on renal biopsy as no serum or biological markers currently exist for definitive confirmation. Currently, the etiology and pathogenesis of the disease remains unclear, although the multiple-hit theory is postulated (Al Hussain *et al.*, 2017) as it is closely related to the pathogenesis of IgAN. Within this framework, Gd-IgA1 is implicated as the initiating factor of multiple-hit IgAN (Suzuki, 2019), wherein Oligosaccharylated IgA1 molecules in the IgA1 hinge region induce immune reactions resulting in the formation of antigen-antibody immune complexes between

Oligosaccharylated IgA1 molecules and anti-glycan antibodies. Subsequent deposition of these complexes in the glomerular mesangial area and activation of the complement pathway, stimulate inflammatory responses, thereby inducing glomerular injury (Suzuki *et al.*, 2011).

Proteinuria, hematuria, and hypertension have been identified as risk factors for the progression and poor prognosis of this disease. Persistent proteinuria and hematuria, the primary clinical manifestations of IgAN, can cause kidney injury, with the scale and duration of proteinuria influencing the progression of IgAN. Studies have demonstrated that patients with 24-UTP levels exceeding 1 gram exhibit a poorer prognosis and a heightened risk of advancing to stage V CKD compared to those with levels below 1 gram (Nagaraju *et al.*, 2018). In a longitudinal study with an average follow-up duration of (14.0 \pm 10.2) years,

involving 112 patients with IgAN, it was observed that those with persistent hematuria progressed more rapidly and had significantly worse outcomes compared to patients with absent or mild hematuria (Sevillano *et al.*, 2017).

Hypertension, as one of the clinical manifestations of IgAN, exacerbates glomerular damage through hemodynamic changes, thereby worsening the disease's progression and prognosis. Persistent hypertension intensifies damage to the glomeruli, tubules, and renal vessels, further impairing renal function. Studies indicate that the presence of hypertension at the initial stage of IgAN significantly increases risks and worsens the prognosis compared to patients without hypertension (Berthoux *et al.*, 2011). The Kidney Disease Improving Global Outcomes (KDIGO) guidelines (Rovin *et al.*, 2021) recommend stringent blood pressure control for patients with proteinuria exceeding 1 g/day, setting a target below 125/75 mmHg. Therefore, effective control of blood pressure is particularly important in the treatment of IgAN.

Research has highlighted a significant correlation between proteinuria and GFR. Consistently low levels of proteinuria have been shown to slow the deterioration of renal function (Liu *et al.*, 2020). A study revealed that changes in SCr and GFR may affect the Oxford Pathologic Grade (MESTC) of the kidney in patients with IgAN (Monteiro *et al.*, 2019), with SCr increasing in proportion to the odds of E1 formation, while the odds of C increased 2.8-fold for each unit increase in SCr. Each unit increase in GFR was associated with a 6% reduction in T2 and a 4% reduction in C relative to T0. Therefore, effectively managing and improving SCr and renal filtration rates in patients with IgAN can positively influence their prognosis. Current Western medical approaches to treating IgAN primarily focus on symptomatic and supportive care. In cases of severe disease or rapid progression, treatment may involve the use of hormones or immunosuppressive agents, tailored to the clinical status of the patient. However, these interventions are often associated with significant side effects (Rauen *et al.*, 2015; Floege & Amann, 2016).

IgAN lacks a specific designation in classical TCM texts. However, according to its clinical manifestations, it can be categorized under terms such as “hematuria,” “turbid urine,” “edema,” and “low back pain.” Yu a prominent TCM scholar,

contends that IgAN manifests through various syndromes, among which the syndrome of spleen deficiency and dampness-heat is increasingly prevalent. Its pathogenesis is characterized by the deficiency of spleen and the accumulation of dampness-heat, which will cause kidney deficiency over time, and dampness-heat will also lead to water stagnation and blood stasis. Consequently, toxic pathogens accumulate in the kidney channels, leading to progressive renal damage and exacerbation of the condition. This cyclic process involves a reciprocal influence between congenital and acquired factors, wherein kidney deficiency exacerbates spleen deficiency, damp-heat, and blood stasis, further perpetuating the pathological cycle. Therefore, according to this syndrome, the treatment of invigorating the spleen and supporting the healthy energy, clearing away dampness-heat and expelling turbidity is proposed to control the disease before the occurrence of disease transmission to prevent its further development.

The BZQLD utilizes a blend of traditional Chinese medicinal herbs to address specific symptoms and underlying conditions in patients. Astragalus is a key component, valued for its ability to bolster qi (vital energy) and elevate yang, which helps induce diuresis and alleviate edema. The classical TCM text *Changsha Yao Jie* describes the benefits of *Codonopsis spilosula*, noting its effectiveness in invigorating the spleen and stomach, replenishing middle qi, and thus regulating the body's energetic flows, which in turn supports the functioning of the five viscera. The *Materia Medica Huiyan* emphasizes the role of *Atractylodes macrocephala* Koidz in invigorating the spleen, enhancing digestion, and dispelling cramps, illustrating its critical role in digestive health and muscle function. Additionally, *Scutellaria baicalensis* is incorporated for its properties of clearing heat and dampness, a common issue in TCM that relates to inflammation and fluid imbalance. Further contributing to the formula, *Poria cocos* and Coix seed promote diuresis and spleen health, essential for fluid regulation and overall energy. Foochow yam rhizome is similarly used for its diuretic properties, assisting in fluid management and dampness diffusion. *Notopterygium incisum* plays a dual role by countering dampness and strengthening the spleen and stomach, crucial for maintaining digestive health and immune function. *Bombyx mori*, known for its

phlegm-dissipating properties, addresses respiratory and digestive tract congestion. Through the synergistic effects of these herbs, the Buzhong Qingli Decoction aims to invigorate qi and spleen, eliminate dampness and heat, and rectify pathogenic factors, providing a holistic treatment approach that addresses both the symptoms and root causes of the condition.

In addition, modern pharmacological studies have demonstrated that *Astragalus membranaceus* can improve the immune function, exert diuretic and hypotensive effect, as well as mitigate urinary protein excretion. Moreover, it is implicated in modulating blood lipids, blood glucose, protein and other metabolic processes, while also demonstrating reparative properties in renal tubules (Liu *et al.*, 2019). Studies on the chemical composition of *Atractylodes macrocephala* Koidz have demonstrated that it improves kidney injury and fibrosis (Liu *et al.*, 2024), and consequently slows the rate of disease progression. Triterpenoids and polysaccharides found in *Poria cocos* have exhibited various biological activities, such as diuresis, renal protection, and so on. They also exhibit specific roles in counteracting tumors, preventing oxidation and regulating immunity. Baicalin is a flavonoid, extracted from *Scutellaria baicalensis* (Jiang *et al.*, 2022; Wang *et al.*, 2024). In animal models it has been demonstrated that baicalin can inhibit cellular inflammation and apoptosis in rats with mesangial proliferative glomerulonephritis by reducing the NLRP3/caspase-1 pathway activation and downregulating NOD-like receptor protein 3, caspase-1 mRNA and protein expression (Zhang *et al.*, 2021).

In this study, a decrease in TCM syndrome scores of 62 patients with IgAN exhibiting the dampness-heat due to spleen deficiency syndrome could be observed after treatment with BZQLD ($p < 0.05$). The finding indicates that BZQLD improved the relevant symptoms and signs of the

study participants. Of note, the treatment with BZQLD have risen the overall response rate in both TCM syndrome efficacy and clinical efficacy of the patients with IgAN, mainly manifesting as the protective effects on the levels of hematuria, proteinuria, SCr and the value of GFR. At the end of follow-up phase, there was no statistical difference in ALT, AST and HGB before and after treatment ($p > 0.05$). Furthermore, no primary endpoint events occurred during the entire follow-up phase of the study, indicating that the study drug in this trial exhibited a satisfactory safety profile.

In conclusion, BZQLD has demonstrated potential in enhancing the TCM symptoms in patients with IgAN, along with reducing urine red blood cell count per high power field, 24-hour UTP, and SCr. Importantly, it also appears to increase the GFR, decelerate its rate of decline, and support the maintenance and improvement of renal function. This multifaceted efficacy enables BZQLD to address several risk factors critical to the prognosis of IgAN. During the follow-up phase of the study, no significant adverse reactions were reported, underscoring the decoction's favorable safety profile. Given its significant clinical efficacy and safety, BZQLD holds substantial clinical value and merits wider adoption in the management of IgAN.

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Conflict of interest

The authors have no conflict of interest.

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