

Original Research Article

Efficacy of Qingying decoction and Wuling powder in the treatment of renal hematuria: A traditional Chinese medicine approach

Rui Tao¹, Shuxiang Yu¹, You Lu^{2*}, Lan Zhai³, Hongsheng Zhang³, Xiao Yang⁴

¹Department of Traditional Chinese Medicine, ²Department of Pharmacy, Emergency General Hospital, Beijing 100028, ³Health Service Center of Nanmofang Community, Chaoyang District of Beijing City, Beijing 100124, ⁴Chang Ying Community Health Service Center, Sanjianfang East Road, Chaoyang District, Beijing 100024, China

*For correspondence: **Email:** earhit@sina.cn

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Abstract

Purpose: To investigate the efficacy of combining Qingying decoction with Wuling powder in the treatment of renal hematuria.

Method: Seventy-six patients diagnosed with renal hematuria in the Emergency General Hospital and Nanmofang Community Health Service Center in Chaoyang District of Beijing, China were randomized equally into study and control groups. Control group received standard Western treatment in addition to Shenyan Rehabilitation tablets while study group received a combination of Qingying decoction and a modified Wuling powder alongside standard treatment for eight weeks. Treatment effectiveness was evaluated using urinary red blood cell count (URBC), urinary albumin-to-creatinine ratio (UACR), urinary β 2-microglobulin (β 2-MG) and α 1-microglobulin (α 1-MG) levels, serum levels of complement components 3 (C3) and 4 (C4), immunoglobulin A (IgA), and Traditional Chinese Medicine (TCM) syndrome scores.

Results: There was a significant difference in total therapeutic effectiveness between study and control groups ($p < 0.01$). Study group showed significantly improved hematuria and total syndrome scores ($p < 0.01$). The study group showed significantly lower URBC, UACR, β 2-MG, α 1-MG, IgA, and C3 levels compared to the control group ($p < 0.05$).

Conclusion: Treatment with Qingying decoction and Wuling powder demonstrates efficacy in managing renal hematuria, regulates urinary red blood cell counts, reduces symptoms, and lowers early renal impairment. Future studies in multiple centers using larger number of patients to determine the mechanisms of these drug actions and interactions and other related factors would be required.

Keywords: Renal hematuria, Renal damage, Ying heat, Qi Phase, Qingying decoction, Wuling powder, Traditional Chinese medicine

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INTRODUCTION

Renal hematuria, originating from the Greek words 'haima' (blood) and 'ouron' (urine), signifies the presence of blood in the urine. This

condition manifests in two forms namely; gross hematuria, where the blood is visible to the naked eye, and microscopic hematuria, detectable only under a microscope. It is a relatively common observation in certain patient

demographics. While the prevalence of asymptomatic microscopic hematuria varies widely between 1.7 to 31.1 %, a prevalence rate of 4 to 5 % is generally accepted in clinical settings. Variation in prevalence rates is attributed to different factors such as the criteria for defining hematuria, frequency of testing, and demographic variables like age, gender, and associated risk factors [1]. The presence of dysmorphic RBCs with irregular contours and shape in the urine characterizes glomerular hematuria [2] and indicates RBCs entry from the glomerular capillary into the urinary space. Therefore, glomerular hematuria is a marker of dysfunction of the glomeruli filtration barrier [3]. The glomeruli filtration barrier is an extremely complex and specialized structure [4], with different constituents and cell types, which allows a free permeability to water, and small and mid-sized plasma solutes, but keeps a highly specialized selectivity for proteins and larger molecules according to size and molecular weight [5]. Currently, mainstream medicine does not offer a specific, effective treatment for renal hematuria. Management strategies primarily focus on addressing the underlying causes and observing the natural course of the condition.

Qingying decoction and Wuling powder have been well-documented in traditional Chinese medicine. Qingying Decoction is traditionally utilized across a spectrum of conditions, from dermatological to acute infections. Clinical trials have indicated that Qingying decoction in addition to conventional treatment is effective in the treatment of sepsis where it not only alleviates symptoms rapidly but also diminishes the occurrence of multiple organ dysfunction syndrome [6]. Also, Wuling powder and its derivatives are known for their roles in managing fluid balance and have been beneficial in conditions like congestive heart failure, obesity, and gastrointestinal disturbances [7]. Modern medicine manages symptoms and disease progression without offering specific therapeutic interventions. Therefore, this study investigated Qingying decoction and Wuling powder in a modified regimen for the treatment of renal hematuria.

METHODS

General information

The study included 76 patients with renal hematuria who were treated between January 2019 and December 2021 at the Emergency General Hospital and Nanmofang Community Health Service Center in Chaoyang District of Beijing, China. Patients were randomly assigned

equally to study and control groups using a random number table method. Study group comprised of 38 patients (13 males and 25 females, age range 32 – 75 years, mean age 43.16 ± 10.28 years, disease duration of 3 – 15 years, and average duration of 6.28 ± 3.20 years), and control group comprising of 38 patients (10 males and 28 females, age range 30 – 75 years, average age 37.78 ± 9.62 years, disease duration of 3 – 12 years, average duration 6.22 ± 4.02 years). There were no significant differences in gender, age, or disease duration between the two groups ($p > 0.05$), ensuring comparability. The study received ethical approval from the Ethics Committee of the Emergency General Hospital and Nanmofang Community Health Service Center in Chaoyang District, Beijing (approval no. K19-10) and conformed to the Declaration of Helsinki [8]. All participants and/or their guardians provided signed written informed consent.

Inclusion criteria

Patients who met the established Western medical diagnostic criteria for renal hematuria [9], patients who correspond with TCM diagnostic categories, specifically the wind heat syndrome or lower jiao damp heat syndrome [10], between 18 and 75 years, glomerular filtration rate (GFR) of 50 mL/min or higher, a 24-hour urinary protein quantification < 500 mg, participants who voluntarily agree to join the study and provide a signed informed consent form.

Exclusion criteria

Pregnant or lactating women, patients with significant primary cardiovascular, digestive, and hematopoietic defects systems that could affect treatment or assessment processes, patients with urinary tract diseases, including urolithiasis, tumors, inflammation, or anatomical abnormalities, allergies to any of the medications used, patients with mental health disorders that may impede cooperative engagement in the study.

Treatments

All participants received standard Western medical treatment, which include adherence to a low-sodium diet, blood pressure management, primarily with calcium channel blockers. If blood pressure control was insufficient, combination therapy was considered, ACEIs and ARBs were avoided, proactive management of potential exacerbating factors, such as infections, overexertion, or intense physical activity.

Control group

Control group received Shenyan Kangfu Tablets (Tianjin Tongrentang Group Co., Ltd., license no. Z10940034), at a dose of 0.48 g per tablet making a total of five tablets thrice daily for 8 weeks.

Study group

In addition to baseline therapy, the study group received a Chinese herbal decoction that combined Qingying decoction and Wuling powder. The preparation was made up of Buffalo horn silk (15 g), Raw Rehmannia (10 g), Xuan Shen (15 g), Tian Dong (10 g), Huang Lian (9 g), Dan Shen (15 g), Bamboo leaves (15 g), Lian Qiao (15 g), Jin Yin Hua (10 g), Raw Bai Zhu (20 g), Fu Ling (20 g), Zhu Ling (15 g), Ze Xie (15 g), Gui Zhi (6 g), Fang Feng (6 g), Chai Hu (10 g), White grass root (30 g), Charred Zhi Zi (10 g). Additional herbs were included as necessary to resolve specific syndromes. The hospital pharmacy prepared the herbal mixture as a water-based decoction, which was administered in two divided doses daily, 30 mins after breakfast and dinner for 8 weeks.

Evaluation parameters/indices

Traditional Chinese medicine (TCM) syndrome scoring

Hematuria severity

Hematuria severity which included gross hematuria (presenting as visibly bloody urine, and considered the most severe manifestation with 3 points assigned); dark yellow urine (with blood, indicative of moderate severity, received 2 points); microscopic hematuria (blood is detectable only under a microscope, and considered the least severe with 1 point assigned) was evaluated before and after treatment.

Additional symptom severity

Symptoms like dry mouth, thirst, weakness in the lumbar region and knees, and edema in the eyelids or lower limbs were evaluated. Severity of symptoms was classified as mild (1 point), moderate (2 points), or severe (3 points). Absence of any of these symptoms was scored as 0 point.

Assessment of tongue and pulse

Condition of the tongue coating and pulse were each scored based on observed severity: mild (1

point), moderate (2 points), and severe (3 points).

The cumulative scoring for all the observed symptoms and conditions provided a comprehensive TCM syndrome score, with the total maximum score attainable being 18 points.

Laboratory test

Urine red blood cell count (URBC)

This test measured the number of red blood cells in the urine, helping to quantify the degree of hematuria. A microscopic examination of urine sediment was used to count cells.

Urine albumin to creatinine ratio (UACR)

Levels of albumin and creatinine were measured and the ratio of albumin to creatinine was calculated. This assessment provides information on kidney function and potential proteinuria.

Urine β 2-microglobulin (β 2-MG)

Concentration of β 2-microglobulin in the urine was measured using immunoassay techniques, providing information on tubular renal function.

Urine α 1-microglobulin (α 1-MG)

Tubular damage and dysfunction was determined using immunoassays.

Serum complements 3 (C3) and 4 (C4)

Serum C3 and C4 was measured using nephelometry and immunoassay.

Immunoglobulin A (IgA)

Concentration of IgA (indicator of renal pathology) in the blood was assessed using immunoassays.

Adverse effects

Adverse effects such as nausea, vomiting, diarrhea, or skin rashes, were compared between two groups.

Efficacy

Effectiveness of treatment was classified as complete recovery (patient exhibits no symptoms, and routine urine tests reveal normal red blood cell counts), markedly effect (significant reduction in red blood cells in the urine, with a decrease of three or more cells per

high-power field (HPF) after treatment), effective (treatment results in moderate reduction in red blood cells, with a decrease of fewer than three cells per HPF in urine examination after treatment), ineffective (no change, or an increase in urine red blood cell after treatment) [9].

Statistical analysis

Data was processed and analyzed using Statistical Packages for Social Sciences (SPSS 19.0, IBM, Armonk, NY, USA). Continuous variables were expressed as mean \pm standard deviation (SD) and were compared using t-tests. Categorical variables are presented using frequency and percentages, and compared using chi-squared (χ^2). $P < 0.05$ was considered statistically significant.

RESULTS

TCM syndrome scores

Study group showed There was a significant reduction in hematuria score compared to the control group ($p < 0.05$). Also, total TCM

syndrome score was significantly lower in study group compared to control group after treatment ($p < 0.05$, Table 1).

Urinary red blood cell counts

Study group showed significant reduction in urinary red blood cell counts before and after the intervention ($p < 0.05$). There was no significant difference in urinary red blood cells in both groups before treatment ($p > 0.05$). There was a significant reduction in urinary red blood cell in study group compared to control group ($p < 0.05$, Table 2).

Early renal injury markers in urine

Study group showed significant reductions in key renal injury markers such as urine albumin-to-creatinine ratio (UACR), urine β 2-microglobulin (β 2-MG), and urine α 1-microglobulin (α 1-MG) after treatment ($p < 0.05$) compared to control group ($p < 0.05$, Table 3).

Table 1: Traditional Chinese medicine (TCM) syndrome scores (mean \pm SD, N = 38)

Parameter	Group			
	Study		Control	
	Before	After	Before	After
Hematuria	1.98 \pm 1.76	0.63 \pm 1.12	1.92 \pm 1.77	1.36 \pm 1.86*
Dry mouth and thirst	2.12 \pm 1.34	0.21 \pm 0.83	2.20 \pm 1.41	1.83 \pm 1.56
Soreness and weakness of lower back and knees	2.25 \pm 1.37	0.72 \pm 1.13	2.20 \pm 1.59	1.52 \pm 1.58
Eyelid lower limb swelling	1.32 \pm 1.15	0.25 \pm 0.87	1.36 \pm 1.02	0.98 \pm 1.26
Tongue coating	2.16 \pm 0.53	0.61 \pm 0.65	2.15 \pm 0.65	1.09 \pm 0.98
Pulse manifestation	2.28 \pm 0.49	0.79 \pm 0.56	2.35 \pm 0.70	0.91 \pm 0.52
Total score	12.17 \pm 1.06	3.22 \pm 1.08	12.08 \pm 1.12	6.89 \pm 1.06**

Note: * $P < 0.05$ vs before treatment, ** $p < 0.05$ vs study group

Table 2: Urinary red blood cell count (mean \pm SD, N = 38)

Group	Urine sediment red blood cell count (cells/HP)			
	Before treatment	t/p	After treatment	t/p
Study	8.48 \pm 2.37	1.44/> 0.05	3.12 \pm 1.14*	2.01/< 0.05
Control	8.35 \pm 2.46		6.97 \pm 1.86**	

Note: ** $P < 0.05$ vs before treatment, ** $p < 0.05$ vs study group

Table 3: Early renal injury markers in urine (mean \pm SD, N = 38)

Group		UACR	T/P	β 2-MG (mg/L)	t/p	α 1-MG (mg/L)	T/P
Study	Before	3.51 \pm 1.65	2.83/<	3.56 \pm 2.18	2.19/<	28.67 \pm 18.96	2.39/<
	After	2.28 \pm 1.26#	0.01	1.97 \pm 1.56**	0.05	18.68 \pm 14.49*	0.01
Control	Before	3.48 \pm 1.32	1.22/>	3.49 \pm 2.14	0.86/>	28.56 \pm 17.89	1.24/>
	After	3.12 \pm 1.35	0.05	2.65 \pm 1.98	0.05	23.93 \pm 13.52	0.05

Note: * $P < 0.05$ vs control group, ** $p < 0.05$ vs control group, # $p < 0.05$

Table 4: Serum IgA, C3, C4 levels (g/L) (mean \pm SD, N = 38)

Group		IgA (g/L)	t/p	C3 (g/L)	t/p	C4 (g/L)	t/p
Study	Before	4.12 \pm 1.29	2.30/	0.95 \pm 0.21	2.01/	0.23 \pm 0.06	1.50/
	After	2.68 \pm 1.02**	<0.05	1.21 \pm 0.27*	<0.05	0.26 \pm 0.04	>0.05
Control	Before	4.14 \pm 1.25	1.29/	0.96 \pm 0.24	1.62/	0.23 \pm 0.04	1.00/
	After	3.24 \pm 1.16	>0.05	1.09 \pm 0.21	>0.05	0.24 \pm 0.03	>0.05

Note: * P < 0.05 vs control group, ** p < 0.05 vs control group

Table 5: Total efficacy rate (n = 38; N, %)

Group	Complete Recovery	Significant Effect	Effective	Ineffective	Total efficacy (%)	χ^2	P-value
Study	8(21.1)	15(39.5)	10(26.3)	5(13.2)	86.84	8.72	<0.01
Control	3(7.9)	7(18.4)	12(31.6)	16(42.1)	57.89		

Serum IgA, C3, C4 levels

There was a significant decrease in serum IgA levels in study group after treatment compared to control group (p < 0.05). Furthermore, serum C3 levels significantly reduced in study group compared to control group (p < 0.05). There was no significant difference in C4 levels in both groups before and after treatment (p > 0.05, Table 4).

Adverse reaction

There were no significant adverse reactions observed in either study or control group.

Efficacy

Study group showed significantly higher efficacy rate compared to control group (p < 0.05, Table 5).

DISCUSSION

Renal hematuria is a common clinical condition with varying causes which may lead to accumulation of extracellular matrix in kidney cells. Without prompt and appropriate intervention, this condition progresses to renal failure. Renal hematuria, typically resulting from glomerular abnormalities, manifests as either isolated hematuria or combined with proteinuria. Pathogenesis is often linked to immune-inflammatory responses that impair the glomerular basement membrane, allowing red blood cells to leak into the urine [11]. As a result, current medical treatment primarily aims to mitigate initiating factors, as a definitive and effective cure remains unclear. There is however no universally accepted standard treatment. Nephritis recovery tablets have gained

recognition in clinical practice for their effectiveness in treating renal hematuria and reducing renal injury. These tablets have been validated as an effective intervention for chronic nephritis presenting with isolated hematuria [12].

Studies indicates that patients with stages 1 and 2 chronic kidney disease have experienced notable reductions in urinary red blood cells after a three-month treatment regimen with these tablets [13]. Additionally, nephritis recovery tablets have demonstrated potential in ameliorating renal conditions in nephropathic rats by decreasing extracellular matrix deposition in the kidneys, reducing renal interstitial edema and inflammation, and curtailing excessive production of inflammatory mediators and collagen in renal tubular epithelial cells. Their therapeutic effects are attributed to multiple mechanisms, including immune modulation, inflammation control, blood viscosity reduction, and enhancement of renal microcirculation [14].

In traditional Chinese medicine (TCM), hematuria is categorized as 'bleeding in urine' or 'urinating blood,' predominantly attributed to the concept of 'heat scorching the blood collaterals. Contemporary TCM theory posits that renal hematuria is intricately connected to heat, deficiency, and stasis. Initially, heat acts as the primary pathogenic factor, which may evolve to include deficiency heat, blood stasis, damp heat, and toxic heat, reflecting progression of the disease. The complex interaction of stasis, heat, and dampness underpins the persistent and challenging nature of renal hematuria [15]. In renal hematuria, a significant number of patients experience persistent wind-heat and blood stasis obstruction within the kidneys. Initial symptoms often include fever and throat pain, with untreated or recurring cases allowing external

pathogens to reside in the throat's protective layer, eventually reaching the kidneys and transforming into heat. This transformation disrupts kidney function in water and fluid regulation, leading to damp-heat and blood stasis, which then results in microscopic hematuria [16].

The concept of 'inducing ying heat into qi phase' originates during the Qing Dynasty, with recent studies providing further insights into this principle. In this investigation, the therapeutic strategy known as "inducing ying heat into qi phase" is employed, targeting the predominant pathogenic factor of heat in renal hematuria. This approach incorporates measures to eliminate heat and pathogenic factors, ensure smooth qi flow, and facilitates expulsion of pathogens. The therapy centers on Qingying decoction, adjusted to reflect the strategy of purging at the nutritive level, cooling the blood, and dispersing heat. Qingying decoction primarily focuses on detoxification and nourishing yin, with water buffalo horn as its chief ingredient. Additional components like *Radix Scrophulariae*, *Rehmannia glutinosa*, and *Asparagus cochinchinensis* work in unison to detoxify, cool the blood, nourish yin, and maintain body fluids. Substances such as *Coptis chinensis*, *Salvia miltiorrhiza*, Honeysuckle, Forsythia, and Bamboo leaves are integrated to calm and purify the heart, promote blood circulation, and address blood stasis and heat. Herbs like *Fangfeng*, *Bupleurum*, *Imperata cylindrica* root, and *Gardenia jasminoides* augment the formula, disperse wind and *qi*, stop bleeding, invigorate blood, resolve stasis, and clear fire and heat from the triple burner. Collectively, this comprehensive prescription unifies various therapeutic effects, including detoxification, Inducing *Ying* heat into *qi* phase, dampness eradication, wind dispelling, stasis resolution, and hemostasis. Recent pharmacological studies have revealed that the root of *Imperata cylindrica* reduces vascular permeability and limits plasma extravasation. It does not only aid in the generation of prothrombin but also plays a crucial role in promoting blood coagulation, stimulating diuresis, fighting inflammation, displaying antibacterial effect, and enhancing immune responses [17].

Gardenia jasminoides has been found to significantly boost proliferation of human endothelial cells, improve blood flow in internal organs and expediting repair of endothelial cells,

thereby contributing to hemostasis [18]. *Saposhnikovia divaricata*, or Fangfeng, exhibits significant antibacterial and anti-inflammatory properties. It shows inhibitory actions against various bacteria, including *Staphylococcus aureus*, Group II hemolytic streptococcus, and *Streptococcus pneumoniae*. Additionally, polysaccharides in Fangfeng enhance immune function by increasing cytotoxic activities of NK cells and splenic lymphocytes [19]. Thus, this study investigated the efficacy of combining Qingying decoction with Wuling powder in the treatment of renal hematuria.

The results of this present study revealed that study group experienced significantly improved outcomes compared to the control group. Urinary β 2-microglobulin (β 2-MG) is recognized as a sensitive marker for evaluating glomerular filtration function. Under normal physiological conditions, production and release of β 2-MG are consistent, allowing it to be freely filtered by the glomeruli. After filtration, 99.9 % of β 2-MG is reabsorbed and catabolized by the proximal renal tubule cells [20]. Also, α 1-microglobulin (α 1-MG) is a small molecular weight glycoprotein produced by the liver and lymphocytes, and found in various bodily fluids and on lymphocyte membranes. It passes through glomerular filtration unimpeded and is predominantly reabsorbed and broken down in the proximal convoluted tubule. Due to its larger molecular size compared to β 2-MG, α 1-MG provides a more sensitive measure for detecting early glomerular filtration damage [21]. However, susceptibility to external factors necessitates the concurrent assessment of α 1-MG and β 2-MG to achieve a more comprehensive evaluation of kidney function. Albumin, produced by the liver, is a key plasma protein that usually does not pass through the glomerular filtration barrier. Primary or secondary glomerular diseases compromise this barrier, leading to increased albumin presence in urine. The urinary albumin-to-creatinine ratio (UACR) is employed to assess urinary albumin levels independent of dietary protein effects, offering a more precise measure of albuminuria. These results revealed that the study group showed significantly lower UACR than the control group. This significant difference suggests a more effective restoration of glomerular filtration integrity in the study group.

The complement system plays a critical role in innate immune defense, with components such as C3 and C4 serving as indices of immune

status. Complement 3 (C3), the most abundant complement protein in serum, is key in initiating both classical and alternative complement activation pathways. Decrease in serum C3 levels and its accumulation in renal mesangial area is considered significant risk factors for exacerbation of IgA nephropathy [22]. After treatment, reduction in IgA levels in study group was significantly better compared to control group, and the increase in serum complement C3 was also significantly higher in study group. Therefore, patients with renal hematuria in study group showed significant improvement in immune markers following treatment.

Limitations of this study

The study population is small and was carried out in two centers. Other cofounding factors including the mechanism of the combinations on biochemical and molecular changes were not determined.

CONCLUSION

Qingying decoction combined with Wuling powder (modified for treating renal hematuria), significantly improves symptoms, kidney-related immune markers, and a high efficacy rate with no significant adverse effect. Further studies in multiple centers using larger number of patients should be conducted to determine the mechanisms of these drug actions and interactions and other related factors.

DECLARATIONS

Acknowledgement

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None provided.

Ethical approval

The Ethics Committee of Emergency General Hospital and Nanmofang Community Health Service Center in Chaoyang District, Beijing, China gave approval for this study (K19-10).

Conflict of Interest

No conflict of interest associated with this work.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Rui Tao and Shuxiang Yu contributed equally to this work.

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