Study on the Clinical Efficacy of Bailing Tablets Combined with Strengthening the Spleen and Kidney in the Treatment of Nephropathy

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To observe and study the clinical efficacy of Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis in the treatment of patients with gouty nephropathy, and to provide a reliable theoretical basis and clinical basis. A total of 120 patients with primary gouty nephropathy diagnosed in our hospital from December 2018 to December 2020 were divided into intervention group and control group (randomized). The control group was treated with Bailing tablets alone, while the intervention group was treated with Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis. Clinical efficacy, syndrome efficacy, renal function, urine protein, immune status, psychological status, etc., were compared between the two groups after treatment. The intervention group significantly improved the clinical overall response rate (93.3 % *vs.* 81.6 %, p<0.05), with a post-treatment creatinine of (127.1±23.1) μmol/l in the intervention group compared to (140.3±37.3) μmol/l in the control group (p<0.05). The cluster of differentiation 4/cluster of differentiation 8 in the treatment group was (1.23±0.17), which was significantly lower than that (1.89±0.18) in the control group (p<0.05). Adverse effects were generally similar between the two groups (p>0.05). The treatment of gouty nephropathy using Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis is clinically important for improving renal function, reducing the occurrence of adverse effects and improving systemic immunity, and is a safe and effective drug for the treatment of gouty nephropathy.

Key words: Bailing tablets, traditional Chinese medicine, blood stasis, gouty nephropathy, cluster of differentiation cells

Gout refers to a variety of metabolic diseases characterized by the deposition of monosodium urate crystals in tissues. On the renal side, gout manifests as acute or chronic gouty nephropathy and urolithiasis[1]. Studies have shown that elevated serum uric acid independently predicts the development of Chronic Kidney Disease (CKD) and gout is present in one-third of patients with chronic renal insufficiency. Bardin *et al.* have reported that one-third of gout patients have hyperechoic ear cords (consistent with crystal deposition), which is associated with an increased risk of hypertension and renal insufficiency[2]. Therefore, early and aggressive intervention in gouty nephropathy can prevent the gradual deterioration of the condition from progressing to renal failure and greatly improve the quality of life of patients.

At present, conventional treatment drugs include non-steroidal anti-inflammatory drugs, corticosteroids, allopurinol, etc., and long-term treatment is required for their recurrent attacks. Since each drug has its own side effects and limitations, careful selection of the drug to be used should always be made. Traditional Chinese Medicines (TCMs) have long been used to treat gout and are characteristically useful for the management of gouty nephropathy. At present, a large number of clinical trials of TCMs have been carried out and widely used in clinical practice for the treatment of gout[3]. At this stage, the effect of Bailing tablets combined with the method of strengthening the spleen, benefiting the

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kidney, removing turbidity and removing blood stasis in the treatment of gouty nephropathy is temporarily unclear, and this study is intended to explore the clinical efficacy of Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis in the treatment of gouty nephropathy, thereby providing a scientific basis for subsequent treatment.

MATERIALS AND METHODS

Study objects:

A total of 120 patients with primary gouty nephropathy from December 2018 to December 2020 in our hospital were selected and after obtaining the informed consent of the patients in advance, the patients were randomly divided into the intervention group and the control group. The control group was treated with Bailing tablets alone, the intervention group was treated with Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis, and those patients who cannot communicate with severe mental illness are not included.

Methods:

All patients were treated with the following; such as guaranteeing a low purine diet, avoiding the use of irritating foods, encouraging increased water intake, guaranteeing urine output and encouraging the use of basic foods to alkalinize urine and maintaining mood. The control group was treated with Bailing tablets alone, while the intervention group was treated with Bailing tablets+The method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis.

Efficacy measures:

It is made according to the "Protocol for the Diagnosis, Syndrome Differentiation and Evaluation of Uric Acid Nephropathy (Trial protocol)[4].

Statistical methods:

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) 24 statistics and the measurement data were analyzed by t-test and expressed as mean±Standard Deviation (SD) (x±s); comparisons between groups were performed by two independent samples t-test and comparisons of count data [n (%)] were performed by χ^2 test when $p<0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

Baseline data was given where 60 patients in the intervention group were of age (35-72 y) and 28 were female. In the control group, 60 patients were of age (34-75 y) and 29 were female (Table 1).

Clinical efficacy between the two groups was compared. According to the clinical symptoms, serum uric acid levels, urinary microalbumin, serum creatinine levels were divided into clinical control, producing effect, effective, ineffective; the intervention group was more effective than the control group ($p<0.05$), as detailed in Table 2.

Syndrome efficacy between the two groups was compared. According to TCM clinical symptoms, signs and syndrome scores were divided into clinical control, producing effect, effective and ineffective; the syndrome efficacy in the intervention group was better than that in the control group ($p<0.05$), as detailed in Table 3.

Renal function between the two groups was compared. When comparing the renal function indicators such as creatinine, urea nitrogen and uric acid between the two groups before and after treatment, there was no obvious difference in each indicator of renal function between the two groups, which was evaluated again after treatment. It can be seen that the recovery of renal function in the intervention group was more obvious than that in the control group ($p<0.05$), as detailed in Table 4.

Beta-2 Microglobulin (β_2-MG) and urine protein levels before and after treatment in the two groups were compared. By comparing β_2-MG, 24 h urine protein of the two groups of patients before and after treatment, it can be seen that the urine protein of the kidney in the intervention group after treatment was lower, as detailed in Table 5.

Peripheral blood lymphocyte subsets between the two groups were compared. By comparing the lymphocyte subsets in peripheral blood before and after treatment between the two groups, we can see that there was no difference between the two groups before treatment, while in the intervention group, the Cluster of Differentiation $CD3^+/CD4^+$ were higher, while $CD4^+/CD8^+$ were lower after treatment, as detailed in Table 6.

Adverse reactions between the two groups were compared. Adverse effects such as nausea and vomiting, diarrhea, skin rash, and loss of appetite were compared between the two groups, and the incidence of total adverse effects was not significantly different between the two groups[5] (Table 7).

TABLE 1: BASELINE DATA OF THE TWO GROUPS

	Intervention group (n=60)	Control group (n=60)	t/χ^2	p
Age	53.1±16.1	52.5±17.9	0.20	0.83
Gender (female)	28 (%)	29 (%)	0.03	0.86
Complication				
Hypertension	32 (53.3 %)	30 (50.0 %)	0.14	0.71
Coronary Heart Disease (CHD)	24 (40 %)	26 (43.3 %)	0.30	0.58
Diabetes mellitus	33 (55.0 %)	30 (50 %)	0.21	0.65
Tumor	3 (5.0 %)	2 (3.3 %)	0.14	0.71

TABLE 2: COMPARISON OF CLINICAL EFFICACY BETWEEN THE TWO GROUPS

	Clinical controls	Producing effect	Effective	Ineffective	Total effective rate
Intervention group	18 (30.0 %)	25 (41.6 %)	14 (23.3 %)	4 (6.7 %)	56 (93.3 %)
Control group	14 (23.3 %)	20 (33.3 %)	15 (25 %)	11 (18.3 %)	49 (81.6 %)
χ^2					4.62
p					0.03

TABLE 3: COMPARISON OF SYNDROME EFFICACY BETWEEN THE TWO GROUPS

	Clinical cure	Producing effect	Effective	Ineffective	Overall satisfaction rate
Intervention group	19 (31.6 %)	18 (30.0 %)	20 (33.3 %)	3 (5.0 %)	57 (95.0 %)
Control group	12 (20 %)	22 (36.7 %)	16 (26.7 %)	10 (16.7 %)	50 (83.3 %)
χ^2					4.33
p					0.04

TABLE 4: COMPARISON OF RENAL FUNCTION BETWEEN THE TWO GROUPS

		Intervention group (n=60)	Control group (n=60)	t	p
Creatinine (μmol/l)	Before treatment	167.1±26.1	158.2±27.3	1.82	0.07
	After treatment	127.1±23.1	140.3±37.3	-2.22	0.02
Urea nitrogen (μmol/l)	Before treatment	15.6±5.1	16.1±4.4	-0.57	0.56
	After treatment	7.4±3.6	9.3±3.9	-2.77	0.01
Uric acid (μmol/l)	Before treatment	567.1±56.1	557.6±58.2	0.91	0.36
	After treatment	457.1±46.4	483.2±56.2	-2.83	0.01

TABLE 5: COMPARISON OF β_2-MG AND 24 h URINE PROTEIN LEVELS BETWEEN THE TWO GROUPS

		Intervention group (n=60)	Control group (n=60)	t	p
β_2-MG (mg/l)	Before treatment	4.01±0.47	4.04±0.66	-0.28	0.77
	After treatment	2.27±0.06	3.00±0.07	-66	0.000
24 h Total protein (TP) (g/24 h)	Before treatment	1.26±0.08	1.27±0.07	-0.91	0.36
	After treatment	0.66±0.02	0.80±0.01	-5.31	0.000

TABLE 6: COMPARISON OF PERIPHERAL LYMPHOCYTE SUBSETS BETWEEN THE TWO GROUPS

		Intervention group (n=60)	Control group (n=60)	t	p
$CD3^+$	Before treatment	59.36±3.23	58.35±4.12	1.49	0.14
	After treatment	69.36±4.12	59.18±4.01	13.37	0.001
$CD3^+/CD4^+$	Before treatment	25.28±2.98	25.34±3.58	-0.1	0.92
	After treatment	36.32±3.01	29.81±4.56	9.92	0.001
$CD4^+/CD8^+$	Before treatment	2.79±0.13	2.75±0.13	1.68	0.09
	After treatment	1.23±0.17	1.89±0.18	-20	0.0001

TABLE 7: COMPARISON OF ADVERSE EFFECTS BETWEEN THE TWO GROUPS

	Nausea and vomiting	Diarrhea	Skin rash	Loss of appetite	Incidence of adverse reactions
Intervention group	5 (%)	1 (%)	1 (%)	1 (%)	8 (13.3 %)
Control group	4 (%)	4 (%)	1 (%)	5 (%)	12 (20 %)
χ^2					0.96
p					0.32

The etiopathogenesis of gouty nephropathy is extremely complex and the specific pathogenesis of gouty nephropathy is not clear in western medicine. At present, the kidney is the main organ for urate excretion and the urate excretion fraction is determined by glomerular filtration and tubular reabsorption and secretion. Uric acid is deposited in the kidney in various segments of the renal tubules, obstructing the tubules and causing them to dilate, atrophy and even causing fibrosis and necrosis, thus leading to gouty nephropathy[6]. Studies have shown that uric acid crystals have been shown to initiate Interleukin-1 Beta (IL-1β)-mediated inflammation by activating the Nod-Like Receptor Protein 3 (NLRP3) inflammasome[7]. In addition, the expression of lipid metabolism was increased in gouty nephropathy, which may mediate the progression of gouty nephropathy through Phospholipases A2 (PLA2) activation, β-oxidation and activation. Shao *et al.* found that the fecal microbiome and metabolome of patients with gout can be characterized by the disturbance of metabolites involved in the excretion of uric acid and changes in amino acids directly responsible for purine nucleoside biosynthesis, but also by the enrichment of opportunistic pathogens and the reduction of alpha diversity[8]. Western medical treatments are mainly anti-inflammatory, analgesic, uric acid lowering, nascent drugs and other treatments[9,10]. However, the high cost and inherent deficiencies of biopharmaceuticals limit the application of these drugs. The currently available first-line drugs for the treatment of gouty arthritis are associated with multiple adverse effects. Therefore, identifying alternative therapeutic strategies is particularly urgent and important.

Gouty nephropathy appears in TCMs to be mainly caused by deficiency of spleen and kidney, and also by improper diet, cementation of phlegm and stasis for days and a long time, and injury to the kidney[11,12]. The TCM Bailing tablets included in this study contain the active medicinal components of *Cordyceps sinensis*, which has a medicinal history in China for more than 2000 y and possesses various biological activities, and its pharmacological effects involve immunomodulation, anti-oxidation, anti-inflammation, protection of renal function, etc.,[13,14], and the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis is based on clearing heat and eliminating dampness, invigorating spleen and eliminating dampness, and cooling blood and relieving pain[15]. Numerous studies have confirmed the advantages of TCMs for recurrent gouty nephropathy[16,17], many Chinese herbs and their active ingredients can fight gout induced by uric acid crystals and have advantages of low toxicity, etc. The above studies are basically consistent with the results of this study, which indicates that the TCM treatment of Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis, which has an improved effect on clinical symptoms of gouty nephropathy, can restore kidney function and can elevate patient immune function.

There are some limitations in the present study. Because our study had a small sample size, only 120 patients and there was individual variation in patients, the trial results were not very convincing. Future design of scientifically rigorous large sample randomized

controlled experiments is necessary.

Bailing tablets combined with the method of strengthening the spleen, benefiting the kidney, removing turbidity and removing blood stasis can alleviate clinical symptoms, restore renal function and elevate immune function of patients with gouty nephropathy, and other effects.

Author's contributions:

Wenzhong Xiong and Jing Zhou contributed equally to this work.

Conflict of interests:

The authors declared no conflict of interest.

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