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Original Article

Effect of Tripterygium wilfordii polyglycoside tablets on serum inflammatory factors and T cells in patients with chronic nephritis

Qingzhen Li[1], Yong Huang[1], Peipei Liu[1], Hui Yuan[2], Jisheng Zhao[3]

[1]Department of Nephrology, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi Province, China; [2]Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi Province, China; [3]Zhao Jisheng Famous Traditional Chinese Medicine Studio, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi Province, China

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Abstract: Objective: Investigate the effect of Tripterygium wilfordii polyglycoside tablets on serum inflammatory factors and T cells in patients with chronic nephritis. Methods: A total of 89 patients with chronic nephritis were randomly divided into a control group (44 cases, treated with irbesartan hydrochlorothiazide combined with dipyridamole) and an observation group (45 cases, treated with Tripterygium wilfordii polyglycoside tablets based on irbesartan hydrochlorothiazide and dipyridamole like the control group). Patients in both groups were treated for two months. The renal function, inflammatory factors, the proportion of T lymphocyte subsets, and 24 h urinary protein quantification (24 h Upro) of patients with hemodialysis were compared between the two groups before and after treatment. The occurrence of adverse reactions was recorded. Results: SCR, BUN levels, 24 h Upro, serum hs-CRP, TNF-α, and IL-8 levels in the two groups after treatment were lower than those before treatment, and those of the observation group were lower than those of the control group (all $P<0.05$). After treatment, the CD4+ ratio and CD4+/CD8+ ratio of the two groups of patients increased, while the CD8+ ratio decreased. The changes in the observation group were greater than those in the control group (all $P<0.05$). There was no significant difference in the incidence of total adverse reactions between the two groups during treatment ($P>0.05$). Conclusion: Treatment combined with Tripterygium wilfordii polyglycosides can significantly alleviate the inflammatory state of patients with chronic glomerulonephritis, reduce the level of proteinuria, and improve renal function. Tripterygium wilfordii polyglycosides can improve immune function of the body and has high safety.

Keywords: Chronic nephritis, Tripterygium glycosides tablets, inflammatory factors, T lymphocytes

Introduction

Chronic nephritis is a common chronic kidney disease, the most common of which is chronic glomerulonephritis. Patients with chronic nephritis can have a large amount of proteinuria and hematuria. If patients are not treated in time, edema can occur and aggravate their condition [1, 2]. An immunosuppressant is a standard treatment, and this may reduce some patients' medication compliance because of the apparent adverse reactions [3].

According to traditional Chinese medicine, chronic nephritis belongs to the category of "edema" and "turbid urine", which should be treated mainly by removing dampness and detumescence [4, 5]. Tripterygium wilfordii polyglycoside is a fat-soluble mixture extracted and refined from the root of Celastraceae plant Tripterygium wilfordii. It has the effects of dehumidification, detumescence, expelling wind, and detoxification. Modern pharmacologic studies show that it also has specific anti-inflammatory and immunomodulatory effects [6]. There are many studies on the treatment of chronic nephritis with Tripterygium Glycosides tablets. Still, most of them focus on improving renal function in patients with chronic nephritis [7, 8]. Simultaneously, there are few studies on the immune function and inflammatory state of patients with chronic nephritis. Our hospital

tried to use Tripterygium wilfordii polyglycosides in the adjuvant treatment of patients with chronic glomerulonephritis, which showed an excellent therapeutic effect. Adjuvant therapy with Tripterygium wilfordii polyglycosides reduced the inflammatory state and improved the body's immune function. This study aimed to investigate the effects of Tripterygium wilfordii polyglycosides tablets on serum inflammatory factors and T cells in patients with chronic nephritis.

Materials and methods

General information

In this prospective study, about 89 patients with chronic nephritis treated in our hospital from November 2018 to January 2020 were randomly divided into a control group (44 cases, treated with irbesartan hydrochlorothiazide combined with dipyridamole) and an observation group (45 cases, treated with irbesartan hydrochlorothiazide + dipyridamole combined with Tripterygium Glycosides tablets) according to the random number table method. The medical ethics committee of our hospital approved this study.

Inclusion criteria: (1) patients aged 28-65 years old; (2) patients diagnosed with glomerulonephritis according to various clinical examinations; (3) patients with 24 h urinary protein (24 h Upro) >3.5 g, plasma albumin <30 g/L; (4) patients who signed the informed consent.

Exclusion criteria: (1) patients with acute infection; (2) patients with a history of immunosuppressant use two weeks before the enrollment; (3) patients with immune system or blood system diseases; (4) patients with a malignant tumor or severe cardiovascular and cerebrovascular diseases; (5) patients allergic to drugs in this study.

Method

The control group was treated with Irbesartan Hydrochlorothiazide combined with dipyridamole. Irbesartan Hydrochlorothiazide tablets (Nanjing Zhengda Tianqing Pharmaceutical Co., Ltd., H20057227, specification: each tablet contains irbesartan 150 mg, Hydrochlorothiazide 12.5 mg) were taken orally two tablets/time, three times/d. Tripterygium glycosides tablets were added in the observation group's treatment compared with the treatment in the control group (Lunan Houpu Pharmaceutical Co., Ltd., Z37020344, specification: 10 mg). Tripterygium glycosides tablets are taken orally 20 mg/time, three times/d. Two groups of patients were treated continuously for two months.

Outcome measures

Main outcome measures: (1) About 5 ml of venous blood was collected before and two months after the treatment, of which 3 ml venous blood was centrifuged to separate serum for standby. The levels of serum creatinine (SCR), blood urea nitrogen (BUN), and other renal function indicators were detected by an automatic biochemical analyzer (Shandong Boke Biological Industry Co., Ltd., Model: BK-280, Origin: China).

(2) The serum levels of hs-CRP, TNF-α, and IL-8 were detected by ELISA.

(3) The remaining 2 mL venous blood was used to detect the proportion of T lymphocyte subsets (CD4+, CD8+) and calculate the ratio of CD4+/CD8+ by flow cytometry (BD company, USA, Model: FACSCalibur, Origin: USA) and its auxiliary reagents.

Secondary outcome measures: (1) The 24 h Upro levels of the two groups before and after the treatment were detected and compared by an automatic biochemical analyzer.

(2) Adverse reactions such as nausea and vomiting, dizziness and headache, elevated transaminase, and skin rash, were recorded in the two groups during the treatment. The incidence of adverse reactions = the number of adverse reactions/total cases × 100%.

Statistical analysis

SPSS 20.0 was used for statistics, and the count data were expressed as the number of cases n (%). χ^2 test was used, and the measured data were represented by mean ± standard deviation ($\bar{x}$ ± sd). The paired t-test was used for comparison before and after the treatment, and an independent t-test was used to compare the two groups. Statistical significance was set at $P<0.05$.

Table 1. Baseline data of the two groups (n, $\bar{x}$ ± sd)

	Observation group (n=45)	Control group (n=44)	χ^2/t	P
Gender (n)			0.109	0.741
Male	24	25		
Female	21	19		
Age (years)	44.4±5.3	45.2±6.8	0.618	0.538
Course of the disease (n)	4.22±1.33	4.76±1.94	1.528	0.130
24 h Upro (g)	3.98±0.35	4.04±0.44	0.711	0.479
Plasma albumin level (g/L)	23.30±3.49	24.04±4.33	0.886	0.378
Basic diseases (n)			0.782	0.676
Diabetes	4	2		
Hypertension	7	6		
Hyperlipidemia	2	3		

Note: 24 h Upro: 24 h urinary protein quantification.

Table 2. Renal function in the two groups before and after treatment ($\bar{x}$ ± sd)

Groups	Scr (μmol/L)	BUN (mmol/L)
Observation group (n=45)		
Before treatment	95.48±9.94	9.05±1.77
After treatment	75.59±6.48[a,b]	6.60±1.30[a,b]
Control group (n=44)		
Before treatment	94.88±7.85	8.88±1.64
After treatment	82.56±7.59[a]	7.46±1.04[a]

Note: Compared with those before treatment, [a]P<0.05; compared with the control group, [b]P<0.05. Scr: serum creatinine; BUN: blood urea nitrogen.

Results

Baseline data

There was no significant difference in the baseline data between the two groups (all P>0.05). They were comparable between the two groups. See **Table 1**.

Renal function

Scr and BUN levels had no significant differences between the two groups before treatment (all P>0.05). After treatment, the Scr and BUN levels in the two groups were lower than those before treatment, and those in the observation group were lower than those of the control group (all P<0.05). See **Table 2**.

Inflammatory factors

Before the treatment, there was no significant difference in serum hs-CRP, TNF-α, or IL-8 levels between the two groups (all P>0.05). The serum hs-CRP, TNF-α, and IL-8 levels of the two groups after treatment were lower than those before treatment, and those of the observation group were lower than those of the control group (all P<0.05). See **Table 3**.

Percentage of T lymphocyte subsets

Before treatment, there were no significant differences in the proportion of CD4+ or CD8+ and CD4+/CD8+ ratio between the two groups (all P>0.05). After treatment, the CD4+ ratio and CD4+/CD8+ ratio of the two groups were increased, while the proportion of CD8+ was decreased. The changes in the observation group were more pronounced (all P<0.05). See **Table 4**.

24 h Upro

The 24 h Upro of the observation and control groups were (3.98±0.35) g and (4.04±0.44) g respectively before the treatment. The 24 h Upro of the two groups were (1.40±0.22) g and (2.22±0.38) g respectively after the treatment. The 24 h Upro of the two groups after treatment was lower than that before treatment, and that of the observation group was lower than that of the control group (P<0.05). See **Figure 1**.

Adverse reactions

There was no significant difference in the total incidence of adverse reactions between the two groups (P>0.05). See **Table 5**.

Discussion

Chronic glomerulonephritis is the most common clinical type of chronic nephritis. The specific pathogenesis has not been fully elucidated, but studies have shown that an inflammatory reaction and immune response disorder are closely related to chronic glomerulonephritis occurrence [9].

Studies have shown that the serum levels of inflammatory factors in patients with chronic nephritis are abnormally higher than those in

Table 3. Levels of serum inflammatory factors before and after treatment in two groups ($\bar{x}$ ± sd)

Groups	hs-CRP (mg/L)	TNF-α (ng/L)	IL-8 (ng/L)
Observation group (n=45)			
Before treatment	2.97±0.68	167.55±20.03	3.23±1.20
After treatment	1.03±0.35[a,b]	103.39±13.22[a,b]	1.44±0.64[a,b]
Control group (n=44)			
Before treatment	2.88±0.73	166.97±18.94	3.55±1.38
After treatment	1.84±0.40[a]	124.56±14.20[a]	2.30±0.79[a]

Note: hs-CRP: high sensitivity C-reactive protein; TNF-α: tumor necrosis factor; IL-8: interleukin-8. Compared with those before treatment, [a]P<0.05; compared with the control group, [b]P<0.05.

Table 4. The proportion of T lymphocyte subsets before and after-treatment in the two groups ($\bar{x}$ ± sd)

Group	CD4+ (%)	CD8+ (%)	CD4+/CD8+
Observation group (n=45)			
Before treatment	30.30±5.44	34.48±4.70	0.88±0.19
After treatment	35.89±4.30[a,b]	27.46±4.57[a,b]	1.30±0.32[a,b]
Control group (n=44)			
Before treatment	30.84±5.95	34.95±5.11	0.87±0.21
After treatment	32.98±4.80[a]	30.04±4.38[a]	1.09±0.28[a]

Note: Compared with those before treatment, [a]P<0.05; compared with the control group, [b]P<0.05.

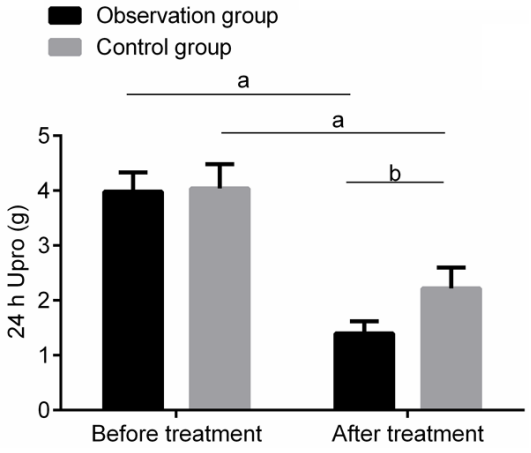

Figure 1. Comparison of 24 h Upro before and after treatment between the two groups. Compared with those before treatment, [a]P<0.05; compared with the control group, [b]P<0.05. 24 h Upro: 24 h urinary protein quantification.

ordinary people [10, 11]. Our results showed that the serum hs-CRP, TNF-α, and IL-8 levels in the two groups after treatment were lower than those before treatment. The levels of serum hs-CRP, TNF-α, and IL-8 in the observation group were lower than those of the control group, suggesting that after the treatment, serum inflammatory factors in patients with chronic glomerulonephritis are decreased. The combination of Tripterygium wilfordii polyglycosides provided definite relief of the inflammatory reaction. Wang et al. also did similar studies, which also found that Tripterygium wilfordii polyglycosides can reduce the level of serum inflammatory factors in patients with chronic glomerulonephritis and alleviate the level of inflammatory reaction [12]. Modern pharmacologic studies also showed that Tripterygium wilfordii polyglycosides have obvious anti-inflammatory effects, so the combination of Tripterygium wilfordii polyglycosides can more significantly alleviate the body's inflammatory reaction [13, 14].

T lymphocytes are the main effector cells that regulate the immune state of the body. Under normal circumstances, CD4+ and CD8+ are in a dynamic balance, and they restrict each other to maintain the normal immune function of the body [15, 16]. Under pathological conditions, the balance between the two is broken, and the immune function is disordered [17]. However, the immune function of patients with chronic glomerulonephritis is disordered, which is mainly manifested by a decrease of the proportion of CD4+ T lymphocytes and an increase of the proportion of CD8+ T lymphocytes [18]. This study showed that after treatment, the proportion of CD4+ and CD4+/CD8+ in the two groups increased, and the proportion of CD8+ decreased. The changes in the observation group were more evident than those of the control group. The differences were statistically significant, suggesting that the improvement effect of Tripterygium wilfordii polyglycoside on patients' immune function with chronic glomerulonephritis is stronger. Modern pharmacological studies show that Tripterygium wilfordii polyglycosides have a pronounced immunoregulatory effect and can enhance the immune function of model rats

Table 5. Incidence of adverse reactions in the two groups during the treatment (n, %)

Groups	Nausea and vomiting	Dizziness and headache	Elevated transaminase	Rash	Total incidence
Observation group (n=45)	2 (4.44)	1 (2.22)	0 (0.00)	1 (2.22)	4 (8.89)
Control group (n=44)	2 (4.55)	2 (4.55)	1 (2.27)	1 (2.27)	6 (13.64)
χ^2					0.503
P					0.478

[19]. Zhu et al. also found that for patients with glomerulonephritis, the combination of Tripterygium wilfordii polyglycosides helped promote the body's initially disordered immune function to return to a normal state [20].

In patients with chronic glomerulonephritis, the glomerular filtration function is impaired and a large amount of proteinuria occurred. The renal function is significantly decreased. 24 h Upro is the most objective assessment of urinary protein. The high level of 24 h Upro suggests more proteinuria and more serious renal function damage [21]. In this study, the levels of 24 h Upro, Scr, and BUN in the two groups after the treatment were lower than those before treatment, and those in the observation group were lower than those of the control group, suggesting that the combination of Tripterygium wilfordii polyglycosides can more effectively reduce the urine protein level of patients with chronic glomerulonephritis and improve renal function. Zhan et al. did a similar study, which also found that the urine protein of patients with chronic glomerulonephritis was significantly reduced, and the glomerular filtration function was also significantly improved after the combined use of Tripterygium wilfordii polyglycosides [22]. In terms of adverse reactions, no severe adverse reactions occurred in the two groups during treatment. The total incidence of adverse reactions had no significant difference between the two groups, which is reassuring for the safety of Tripterygium wilfordii polyglycosides.

However, this study is a single-center randomized controlled study with a limited sample size, and only compared the effect before and two months after the treatment. The effect of Tripterygium wilfordii polyglycosides on long-term renal function and immune function of patients with chronic nephritis still needs to be further studied.

In conclusion, the combined use of Tripterygium wilfordii polyglycosides can more significantly alleviate the inflammatory state of patients with chronic glomerulonephritis, reduce the level of proteinuria, improve renal function, and more effectively improve the body's immune function. The combined use of Tripterygium wilfordii polyglycosides has high safety, and is worthy of clinical promotion.

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Disclosure of conflict of interest

None.

Address correspondence to: Peipei Liu, Department of Nephrology, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, No. 445 Bayi Avenue, Nanchang 330006, Jiangxi Province, China. Tel: +86-15279196091; E-mail: drlpeipei@yeah.net

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