

Original Article

Clinical effect of prednisone combined with tripterygium wilfordii polyglycoside on nephrotic syndrome: renal function and serum inflammatory factors

Zhong-Hui Chen, Chang-Dong Shu, Yan Hu, Jing He, Ji-Ben Mei

Department of Nephrology, Xuancheng People's Hospital, Xuancheng 242300, Anhui Province, China

Received June 10, 2020; Accepted August 10, 2020; Epub January 15, 2021; Published January 30, 2021

Abstract: Objective: The purpose of this study was to explore the clinical effect of prednisone combined with tripterygium wilfordii polyglycoside on nephrotic syndrome as well as their effects on renal function and serum inflammatory factors. Methods: The medical records of 107 patients with nephrotic syndrome in our hospital from June 2018 to September 2019 were collected retrospectively. On the basis of treatment option, they were randomly divided into group A received prednisone tablets only, and group B treated with prednisone and tripterygium wilfordii polyglycoside tablets. The treatment efficacy, renal function indexes, plasma albumin, 24 h urine protein, serum inflammatory factor levels, adverse reactions, and disease recurrence were compared between the two groups. Results: (1) The total response rate in group B was 94.44%, higher than 71.70% in group A ($P<0.05$). (2) After treatment, BUN, SCr, TNF- α , IL-6 and hs-CRP levels in group B were lower than those in group A ($P<0.05$). Group B also exhibited lower levels of protein excretion and higher level of plasma albumin than group A after 24 h of treatment ($P<0.05$). The incidence of adverse reactions in group B was 3.70%, lower than 17.87% in group A ($P<0.05$). (6) The disease recurrence rate in group B was 1.85%, lower than 16.98% in group A ($P<0.05$). Conclusion: Prednisone combined with tripterygium wilfordii polyglycoside has significant clinical efficacy and high safety, which is beneficial to improving renal function and reducing the body's inflammatory response and the disease recurrence rate.

Keywords: Nephrotic syndrome, prednisone tablets, tripterygium wilfordii polyglycoside tablets, renal function, serum inflammatory factors

Introduction

Nephrotic syndrome is a kidney disorder that causes the body to expel too much protein in the urine. It occurs as a result of increased glomerular basement membrane permeability and decreased glomerular filtration. It evolves quickly, and is easy to relapse, leading to high mortality rate [1-3].

At present, the pathogenesis of nephrotic syndrome has not been fully clarified at home and abroad. Most scholars have explained it from the aspects of inflammatory response, non-immune mechanism, immune abnormality and molecular genetics, which are individually or jointly involved in the occurrence of nephrotic syndrome [4-6]. Glucocorticoid is the first line treatment for this disease, but most clinical practice indicates that the improper use of hormones is more likely to cause adrenal corti-

cal dysfunction. Once discontinued, the compensatory function is reduced, leading to the relapse [7]. At the same time, since glucocorticoids affect a variety of biological processes including growth, metabolism, development, behavior, and immune function, it is necessary to pay attention to the pharmacokinetic mechanism of the hormones [8]. In recent years, with the continuous deepening of Chinese medicine research, the application of Chinese medicine has been widely used in various clinical fields. In traditional Chinese medicine (TCM), nephrotic syndrome was categorized as "consumptive disease", "turbid urine", and "edema", which is caused by the invasion of foreign pathogens as well as spleen and kidney deficiency. Therefore, tripterygium wilfordii polyglycoside tablets were recommended for the treatment [9, 10]. Tripterygium wilfordii is a common herb used in TCM and has anti-inflammatory and immunosuppression effects. Tripterygium wilfordii can

Effect of prednisone combined with tripterygium wilfordii polyglycoside

improve proteinuria by repairing glomerular basement membrane [11, 12].

In clinical studies, high-dose glucocorticoids or glucocorticoids combined with immunosuppressive drugs were usually used to treat nephrotic syndrome. However, there are also disadvantages such as high incidence of adverse reactions and high recurrence rate after drug withdrawal [13]. Therefore, this study advocates the combination of TCM on the basis of glucocorticoids, which is innovative and feasible.

Materials and methods

Subjects

The clinical data of 107 patients with nephrotic syndrome in our hospital from June 2018 to September 2019 were collected retrospectively. Based on the treatment option, they were randomly divided into two groups, 53 patients in group A treated with prednisone tablets, and 54 patients in group B treated with prednisone tablets combined with tripterygium wilfordii glycoside tablets. There were 36 males and 17 females in group A, with the average age of 49.63 ± 3.28 years and the average course of disease of 1.98 ± 0.28 years. There were 39 males and 15 females in group B, with the average age of 49.72 ± 3.22 years and the average course of disease of 2.02 ± 0.25 years. (1) Inclusion criteria: patients who met the diagnostic criteria for nephrotic syndrome [14]; patients who had no contraindications for prednisone tablets and tripterygium glycoside tablets; and patients who had complete medication compliance. This study was approved by the medical ethics committee. All patients signed written informed consent. (2) Exclusion criteria: patients with diabetes; patients with arrhythmia; patients with secondary nephrotic syndrome caused by myeloma nephropathy, purpuric nephritis, diabetic nephropathy, lupus nephritis and other diseases; and patients with barriers to communication were excluded.

Methods

Group A: patients were given high-protein, low-carbohydrate diets, anticoagulation therapy as well as hypotensive and diuretic treatments, while prednisone was administered orally (Shanghai Xinyi Pharmaceutical Factory Co.,

Ltd., H31020675, 5 mg). The initial dosage was 0.5 mg/(kg·d). After continuous use for 8 weeks, the dosage was gradually reduced by 10% to final 10-20 mg/d for 6 months.

Group B: On the basis of treatment in group A, patients in group B were given oral tripterygium wilfordii polyglycoside tablets (Hunan Qianjin Xieli Pharmaceutical Co., Ltd., Z43020138, 10 mg×50). The dosage was controlled to 1.5 mg/(kg·d). One course of treatment lasted for 8 weeks and a total of 3 courses of treatment were given.

Observation indicators

(1) Criteria for efficacy evaluation [15]. Marked Response: symptoms basically disappeared; plasma albumin >30 g/L, and urine protein <0.5 g/24 h. Response: symptoms significantly alleviated; plasma albumin ranged between 25-30 g/L, and the urine protein <1.5 g/24 h. No response: clinical symptoms, plasma albumin level and urinary protein were not improved. Response rate = (Marked response + response)/total cases.

(2) Renal function indices. Before and after treatment, blood urea nitrogen (BUN) and blood creatinine (SCr) were measured using a fully automatic biochemical analyzer.

(3) Quantification of plasma albumin and 24 h urinary protein. Before and after treatment, the two groups of patients were measured by automatic biochemical analyzer for plasma albumin level and 24 h urine protein.

(4) Serum inflammatory factor level [16]. Before and after treatment, 3 ml of fasting venous blood samples were collected and centrifuged at 3000 r/min for 15 min to obtain supernatant. Tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP) were all measured by enzyme-linked immunosorbent assay strictly in accordance with the kit instructions (Beijing Zhongshan Jinqiao Biotechnology Co., Ltd.).

(5) Occurrence of adverse reactions was compared between the two groups.

(6) Disease recurrence within 6 months after treatment was compared between the two groups.

Effect of prednisone combined with tripterygium wilfordii polyglycoside

Table 1. Comparison of baseline data between the two groups [n (%)]/($\bar{x} \pm sd$)

Data		Group A (n=53)	Group B (n=54)	t/ X^2	P
Gender (cases)	Male	36 (67.92)	39 (72.22)	0.236	0.627
	Female	17 (32.08)	15 (27.78)		
Age (year)		49.63 \pm 3.28	49.72 \pm 3.22	0.143	0.886
Course of disease (years)		1.98 \pm 0.28	2.02 \pm 0.25	0.779	0.437
Disease type (cases)					
	Initial treatment	42 (79.25)	45 (83.33)	0.294	0.588
	Retreatment	11 (20.75)	9 (16.67)		
Pathological type (case)					
	Minimal lesion	20 (37.74)	22 (40.74)	0.025	0.658
	Mesangial proliferative nephritis	17 (32.08)	15 (27.78)		
	Focal segmental glomerulosclerosis	10 (18.87)	12 (22.22)		
	Membranous nephropathy	6 (11.32)	5 (9.26)		

Table 2. Comparison of clinical efficacy between the two groups [n (%)]

Group	Number of cases	Marked response	Response	No response	Response rate
Group A	53	21 (39.62)	17 (32.08)	15 (28.31)	38 (71.70)
Group B	54	29 (53.70)	22 (40.74)	3 (5.56)	51 (94.44)*
X^2					9.890
P					0.002

Note: *indicates comparison with group A, $P < 0.05$.

Statistical analysis

SPSS22.0 was used for data analysis. Measurement data were expressed as mean \pm standard deviation (mean \pm SD). Data with normal distribution were subjected to t test, and data with non-normal distribution was subjected to Mann-Whitney U test. Count data were expressed as [n (%)] and compared by X^2 test. $P < 0.05$ indicated statistical significance.

Results

Comparison of baseline data between the two groups

There was no significant difference in terms of gender ratio, age and course of disease, relapse rate, and type of nephrotic syndrome between the two groups ($P > 0.05$) (Table 1).

Comparison of clinical efficacy between the two groups

The total response rate in group B was 94.44%, higher than 71.70% in group A ($P < 0.05$) (Table 2).

Comparison of renal function indices between the two groups

Before treatment, no significant difference was found in BUN and SCr levels ($P > 0.05$). Compared with those before treatment, BUN and SCr levels were significantly decreased after treatment ($P < 0.05$). Compared with group A, BUN and SCr levels were lower in group B ($P < 0.05$) (Figure 1).

Comparison of plasma albumin and 24 h urine protein between the two groups

The two groups exhibited no significant difference in serum albumin and 24 h urinary protein before treatment ($P > 0.05$). Compared with that before treatment, 24 h urinary protein decreased in both groups after treatment, showing significant difference ($P < 0.05$). Compared with that before treatment, serum albumin increased in both groups after treatment, showing significant difference ($P < 0.05$). Compared with group A, group B had lower 24 h urine protein and higher plasma albumin levels after treatment ($P < 0.05$) (Figure 2).

Effect of prednisone combined with tripterygium wilfordii polyglycoside

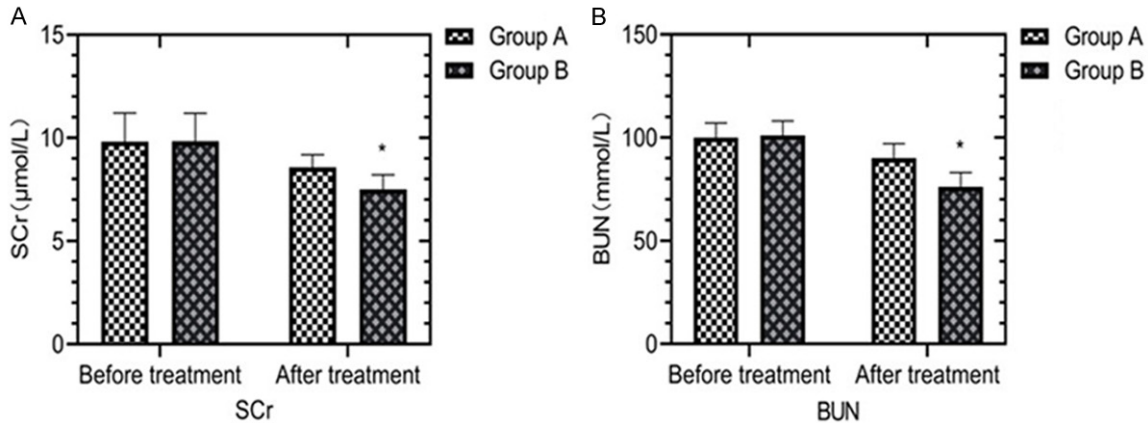


Figure 1. Comparison of renal function indices between the two groups. A. The comparison of SCr levels before treatment in two groups $P>0.05$. After treatment, the SCr level in group B was lower than that in group A, $P<0.05$. B. The comparison of BUN levels in two groups before treatment, $P>0.05$. After treatment, the BUN level in group B was lower than that in group A, $P<0.05$. * Compared with group A, $P<0.05$.

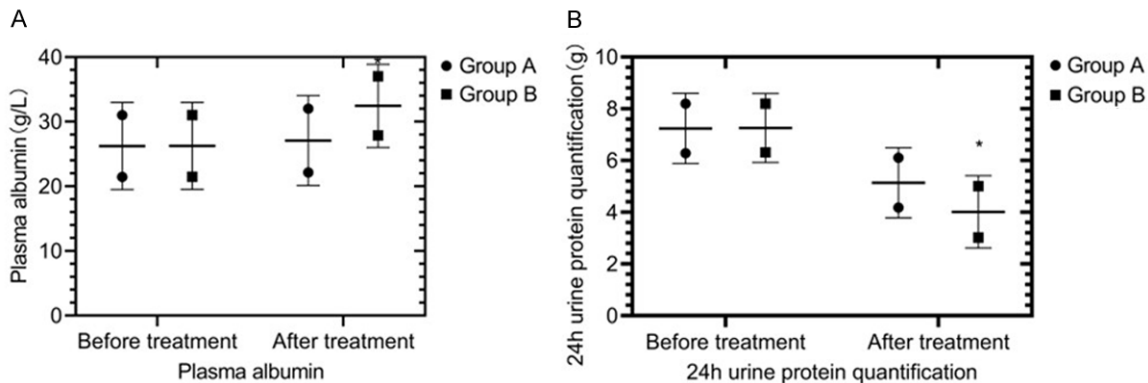


Figure 2. Plasma albumin levels and 24 h urine protein. A. Before treatment, there was no difference in the serum albumin level of the two groups, $P>0.05$. After treatment, the serum albumin in group B was higher than that in group A, $P<0.05$. B. The comparison of 24 h urine protein before treatment, $P>0.05$. After treatment, the 24 h urine protein in group B after 24 h was lower than that in group A, $P<0.05$. * Compared with group A, $P<0.05$.

Comparison of serum inflammatory factors between the two groups

Before treatment, there was no statistically significant difference between two groups in terms of TNF- α , IL-6, and hs-CRP ($P>0.05$). Compared with those before treatment, TNF- α , IL-6, and hs-CRP levels decreased in both groups after treatment, showing significant difference ($P<0.05$). Group B showed lower TNF- α , IL-6, and hs-CRP than group A ($P<0.05$) (Figure 3).

Comparison of adverse reactions between the two groups

During the treatment period, the incidence of adverse reactions in group B was 3.70%, lower than 17.87% in group A ($P<0.05$) (Table 3).

Comparison of disease recurrence between the two groups

The disease recurrence rate in group B was 1.85%, lower than 16.98% in group A ($P<0.05$) (Table 4).

Discussion

Hormones are usually used to treat nephrotic syndrome. Most juvenile patients with nephrotic syndrome have a high sensitivity to hormones, and for relatively older patients, it is difficult to achieve ideal clinical efficacy with hormone therapy alone [17, 18]. Only sufficient hormone and a long treatment period yield ideal efficacy. Therefore, long-term high-dose glucocorticoid therapy was often prescribed for patients [19, 20]. However, long-term high-dose medica-

Effect of prednisone combined with tripterygium wilfordii polyglycoside

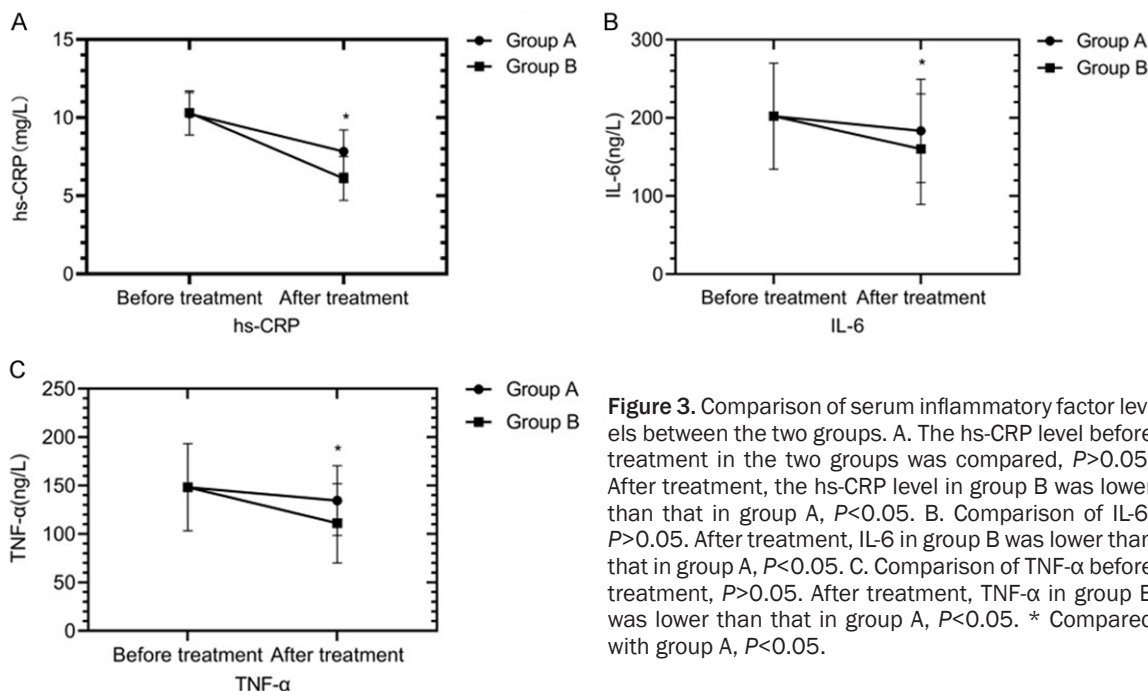


Table 3. Comparison of the incidence of adverse reactions between the two groups [n (%)]

Group	Number of cases	headache	Leukopenia	Gastrointestinal reactions	Incidence
Group A	53	3 (5.66)	4 (7.55)	3 (5.66)	10 (18.87)
Group B	54	1 (1.85)	0 (0.00)	1 (1.85)	2 (3.70)*
χ^2					6.177
P					0.129

Note: *indicates comparison with group A, $P < 0.05$.

Table 4. Comparison of disease recurrence between the two groups [n (%)]

Group	Number of cases	Recurrence rate
Group A	53	9 (16.98)
Group B	54	1 (1.85)*
χ^2		7.226
P		0.007

Note: *indicates comparison with group A, $P < 0.05$.

tion will cause complications such as osteoporosis, secondary immunosuppressive infections, hypertension and hyperglycemia, and after medication withdrawal, the symptoms will reappear. A reasonable combined medication should be explored to reduce the incidence of complications and disease recurrence, and improve the clinical efficacy [21, 22].

TCM believes that nephrotic syndrome is characterized by internal cold and dampness,

caused by spleen and kidney deficiency and invasion of foreign evils [23]. To improve the treatment effect, tripterygium wilfordii polyglycoside tablets were added on the basis of hormone therapy. Results showed that the total response rate in group B was higher than that in group A, and the levels of BUN and SCr as well as 24 h urine protein in group B were lower than those in group A, while the plasma albumin levels were higher than those of group A, suggesting that the combined therapy showed better efficacy, which is conducive to improving renal function. In TCM, tripterygium wilfordii has the effects of reducing swelling and analgesic, removing wind and dampness, and tonifying the blood circulation [24]. Modern pharmacological studies have shown that tripterygium wilfordii polyglycoside tablets are the main active ingredient of tripterygium wilfordii, with an ideal immunosuppressive effect, which can excite the hypothalamus-pituitary-adrenal axis,

promote glucocorticoid synthesis, and promote the proliferation of mesangial cells, thereby improving the permeability of the glomeruli and reducing proteinuria production [25, 26]. Prednisone combined with tripterygium wilfordii polyglycoside tablets can significantly reduce the patient's proteinuria and increase the total protein and serum albumin concentration. This study also showed that the incidence of adverse reactions and disease recurrence rates in group B were lower than those in group A, suggesting that combined treatment has high safety and can also improve disease recurrence. The underlying mechanism may be that tripterygium wilfordii polyglycoside does not bring hormone-like adverse reactions [27].

Inflammation refers to the activation of the mononuclear macrophage system under the stimulation of various chemicals, endotoxins, and microorganisms, and then the inflammatory responses occur with the release of pro-inflammatory cytokines [28]. In patients with nephrotic syndrome, immune function is disordered, and inflammatory cytokines are activated and released into the blood, exacerbating glomerular damage. TNF- α is one of the common inflammatory factors, and its sources include not only infiltrates of inflammatory cells in the kidney, but also proximal tubule epithelial cells and mesangial cells. Therefore, TNF- α plays a crucial role in kidney damage and immune inflammation. IL-6 is an inflammatory mediator. It can bind to IL-6 receptors on the surface of mesangium and promote stromal hyperplasia and mesangial cell proliferation, causing inflammation and immune damage in the kidney. C-reactive protein (CRP) is a homopentameric acute-phase protein, and the level of hs-CRP in patients with nephrotic syndrome is significantly increased. In this study, the levels of TNF- α , IL-6, and hs-CRP in group B were lower than those in group A, suggesting that prednisone tablets combined with tripterygium wilfordii tablets could decrease inflammatory response. Another study found that there was no significant difference in serum inflammatory factor levels between the two groups before treatment ($P>0.05$), whereas after treatment, the observation group had significant data advantages, and the total effective rate of the observation group was higher than that of the control group ($P<0.05$), which was similar to the results of this study [29]. We assume that

tripterygium wilfordii polyglycoside tablets can reduce the deposition of antigen-antibody complexes, so that cell damage is alleviated, and the integrity of the glomerular basement membrane is effectively maintained. The drug can also inhibit the proliferation of cells and induce apoptosis, thus reducing the levels of inflammatory factors such as TNF- α , IL-6, hs-CRP, and slowing down the pathological process.

To sum up, the treatment of nephrotic syndrome with prednisone tablets combined with tripterygium wilfordii glycoside tablets has significant clinical efficacy and high safety, which is conducive to improving renal function, reducing the body's inflammatory response, and reducing the rate of disease recurrence.

Although this research has reached some conclusions, it also has the limitation of small sample size. Therefore, a more comprehensive study with a larger sample size and a longer time is needed.

Disclosure of conflict of interest

None.

Address correspondence to: Zhong-Hui Chen, Department of Nephrology, Xuancheng People's Hospital, Xuancheng District, Xuancheng 242300, Anhui Province, China. Tel: +86-1363-7221430; E-mail: czhcheen@163.com

References

- [1] Downie ML, Gallibois C, Parekh RS and Noone DG. Nephrotic syndrome in infants and children: pathophysiology and management. *Paediatr Int Child Health* 2017; 37: 248-258.
- [2] Iijima K, Sako M and Nozu K. Rituximab for nephrotic syndrome in children. *Clin Exp Nephrol* 2017; 21: 193-202.
- [3] Iijima K, Sako M, Kamei K and Nozu K. Rituximab in steroid-sensitive nephrotic syndrome: lessons from clinical trials. *Pediatr Nephrol* 2018; 33: 1449-1455.
- [4] Warejko JK, Tan W, Daga A, Schapiro D, Lawson JA, Shril S, Lovric S, Ashraf S, Rao J, Hermle T, Jobst-Schwan T, Widmeier E, Majmundar AJ, Schneider R, Gee HY, Schmidt JM, Vivante A, van der Ven AT, Ityel H, Chen J, Sadowski CE, Kohl S, Pabst WL, Nakayama M, Somers MJG, Rodig NM, Daouk G, Baum M, Stein DR, Ferguson MA, Traum AZ, Soliman NA, Kari JA, El Desoky S, Fathy H, Zenker M, Bakkaloglu SA,

Effect of prednisone combined with tripterygium wilfordii polyglycoside

- Müller D, Noyan A, Ozaltin F, Cadnapaphornchai MA, Hashmi S, Hopcian J, Kopp JB, Benador N, Bockenbauer D, Bogdanovic R, Stajić N, Chernin G, Ettenger R, Fehrenbach H, Kemper M, Munarriz RL, Podracka L, Büscher R, Serdaroglu E, Tasic V, Mane S, Lifton RP, Braun DA and Hildebrandt F. Whole exome sequencing of patients with steroid-resistant nephrotic syndrome. *Clin J Am Soc Nephrol* 2018; 13: 53-62.
- [5] McCloskey O and Maxwell AP. Diagnosis and management of nephrotic syndrome. *Practitioner* 2017; 261: 11-15.
- [6] Colucci M, Corpetti G, Emma F and Vivarelli M. Immunology of idiopathic nephrotic syndrome. *Pediatr Nephrol* 2018; 33: 573-584.
- [7] Lovric S, Ashraf S, Tan W and Hildebrandt F. Genetic testing in steroid-resistant nephrotic syndrome: when and how? *Nephrol Dial Transplant* 2016; 31: 1802-1813.
- [8] Kemper MJ, Valentin L and van Husen M. Difficult-to-treat idiopathic nephrotic syndrome: established drugs, open questions and future options. *Pediatr Nephrol* 2018; 33: 1641-1649.
- [9] Olowu WA, Ademola A, Ajite AB and Saad YM. Childhood nephrotic syndrome in tropical Africa: then and now. *Paediatr Int Child Health* 2017; 37: 259-268.
- [10] Pasini A, Benetti E, Conti G, Ghio L, Lepore M, Massella L, Molino D, Peruzzi L, Emma F, Fede C, Trivelli A, Maringhini S, Materassi M, Messina G, Montini G, Murer L, Pecoraro C and Pennesi M. The Italian society for pediatric Nephrology (SINePe) consensus document on the management of nephrotic syndrome in children: Part I - Diagnosis and treatment of the first episode and the first relapse. *Ital J Pediatr* 2017; 43: 41.
- [11] Watanabe A, Feltran LS and Sampson MG. Genetics of nephrotic syndrome presenting in childhood: core curriculum 2019. *Am J Kidney Dis* 2019; 74: 549-557.
- [12] Dogra S and Kaskel F. Steroid-resistant nephrotic syndrome: a persistent challenge for pediatric nephrology. *Pediatr Nephrol* 2017; 32: 965-974.
- [13] Sharif B and Barua M. Advances in molecular diagnosis and therapeutics in nephrotic syndrome and focal and segmental glomerulosclerosis. *Curr Opin Nephrol Hypertens* 2018; 27: 194-200.
- [14] Horinouchi T, Sako M, Nakanishi K, Ishikura K, Ito S, Nakamura H, Oba MS, Nozu K and Iijima K. Study protocol: mycophenolate mofetil as maintenance therapy after rituximab treatment for childhood-onset, complicated, frequently-relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome: a multicenter double-blind, randomized, placebo-controlled trial (JSKDC07). *BMC Nephrol* 2018; 19: 302.
- [15] Trautmann A, Schnaidt S, Lipska-Ziętkiewicz BS, Bodria M, Ozaltin F, Emma F, Anarat A, Melk A, Azocar M, Oh J, Saeed B, Gheisari A, Caliskan S, Gellermann J, Higueta LMS, Jankauskiene A, Drozd D, Mir S, Balat A, Szczepanska M, Paripovic D, Zurowska A, Bogdanovic R, Yilmaz A, Ranchin B, Baskin E, Erdogan O, Remuzzi G, Firszt-Adamczyk A, Kuzma-Mroczkowska E, Litwin M, Murer L, Tkaczyk M, Jardim H, Wasilewska A, Printza N, Fidan K, Simkova E, Borzecka H, Staude H, Hees K and Schaefer F. Long-term outcome of steroid-resistant nephrotic syndrome in children. *J Am Soc Nephrol* 2017; 28: 3055-3065.
- [16] De Castro I, Easterling TR, Bansal N and Jefferson JA. Nephrotic syndrome in pregnancy poses risks with both maternal and fetal complications. *Kidney Int* 2017; 91: 1464-1472.
- [17] Fu HD, Qian GL and Jiang ZY. Comparison of second-line immunosuppressants for childhood refractory nephrotic syndrome: a systematic review and network meta-analysis. *J Investig Med* 2017; 65: 65-71.
- [18] Matsuo T, Tanaka T and Kinomura M. Nephrotic syndrome during the tapering of oral steroids after pathological diagnosis of Kimura disease from a lacrimal gland mass: case report and review of 10 Japanese patients. *J Clin Exp Hematop* 2017; 57: 147-152.
- [19] Varner JD, Matory A and Gbadegesin RA. Genetic basis of health disparity in childhood nephrotic syndrome. *Am J Kidney Dis* 2018; 72: S22-s25.
- [20] Kelddal S, Nykjær KM, Gregersen JW and Birn H. Prophylactic anticoagulation in nephrotic syndrome prevents thromboembolic complications. *BMC Nephrol* 2019; 20: 139.
- [21] Nakamori A, Akagaki F, Yamaguchi Y, Arima R and Sugiura T. Nephrotic syndrome with thrombocytopenia, lymphadenopathy, systemic inflammation, and splenomegaly. *Intern Med* 2018; 57: 1123-1129.
- [22] Wu J, Guo N, Chen X and Xing C. Low triiodothyronine syndrome is associated with platelet function in patients with nephrotic syndrome. *Rev Assoc Med Bras (1992)* 2019; 65: 988-992.
- [23] Sinha A, Gupta A, Kalaivani M, Hari P, Dinda AK and Bagga A. Mycophenolate mofetil is inferior to tacrolimus in sustaining remission in children with idiopathic steroid-resistant nephrotic syndrome. *Kidney Int* 2017; 92: 248-257.
- [24] Watany MM and El-Horany HE. Nephronectin (NPNT) and the prediction of nephrotic syndrome response to steroid treatment. *Eur J Hum Genet* 2018; 26: 1354-1360.

Effect of prednisone combined with tripterygium wilfordii polyglycoside

- [25] Han X, Xiao Y, Tang Y, Zheng X, Anwar M and Qin W. Clinical and pathological features of immunoglobulin A nephropathy patients with nephrotic syndrome. *Clin Exp Med* 2019; 19: 479-486.
- [26] Li Y, He Q, Wang Y, Dang X, Wu X, Li X, Shuai L and Yi Z. A systematic analysis of major susceptible genes in childhood-onset steroid-resistant nephrotic syndrome. *Ann Clin Lab Sci* 2019; 49: 330-337.
- [27] Liu Y, Lai M, Lou Y, Han Q, Yang Q, Chen M, Li J, Wang H, Yan W and Zheng X. Elevation of plasma-soluble HLA-G in childhood nephrotic syndrome is associated with IgE. *Ann Clin Biochem* 2017; 54: 69-75.
- [28] Hoseini R, Sabzian K, Otukesh H, Zafaranloo N, Panahi P, Rahimzadeh N, Nakhaie S and Akhavan Sepahi M. Efficacy and safety of rituximab in children with steroid- and cyclosporine-resistant and steroid- and cyclosporine-dependent nephrotic syndrome. *Iran J Kidney Dis* 2018; 12: 27-32.
- [29] Bierzynska A and Saleem MA. Deriving and understanding the risk of post-transplant recurrence of nephrotic syndrome in the light of current molecular and genetic advances. *Pediatr Nephrol* 2018; 33: 2027-2035.