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Analysis of Tacrolimus Combined with Glucocorticoids for Refractory Nephrotic Syndrome

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Abstract: *Objective:* To analyze changes in liver and kidney function and lipid metabolism in patients with refractory nephrotic syndrome (RNS) after receiving different treatments. *Methods:* A total of 64 patients treated in the Wuwei Hospital of Traditional Chinese Medicine from January 2018 to January 2021 were included in this study. All subjects were diagnosed with RNS and randomly assigned to groups: a control group (32 cases) and an observation group (32 cases). The control group received cyclophosphamide + glucocorticoids, while the observation group received tacrolimus + glucocorticoids, both for six months. The various indicators of the two groups were compared. *Results:* After six months of treatment, the overall clinical efficacy rate of the observation group was significantly higher than that of the control group. Six months post-treatment, levels of serum ALT, AST, BUN, SCr, 24 h UTP, TG, and TC were reduced in both groups compared to baseline levels, with reductions more pronounced in the observation group. Serum ALB levels increased in both groups, with a more significant increase in the observation group. Statistical analysis showed these differences were significant ($P < 0.05$). There were no significant changes in FBG levels in either group ($P > 0.05$). *Conclusion:* For RNS patients, treatment with tacrolimus combined with glucocorticoids significantly reduces liver function damage, improves kidney function and lipid metabolism, and enhances clinical efficacy.

Keywords: Nephrotic syndrome; Refractory; Tacrolimus; Glucocorticoids; Kidney function

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1. Introduction

Refractory nephrotic syndrome (RNS) is a clinical progression stage resulting from the sustained development of various primary renal diseases, making it a common type of urinary system-related disease [1]. Patients with RNS often exhibit clinical manifestations such as massive proteinuria and hyperlipidemia, making treatment challenging and prone to relapse, thus requiring timely and effective therapeutic intervention [2]. Glucocorticoid therapy is a primary treatment for RNS, suppressing immune and inflammatory responses, often combined

with cyclophosphamide. However, some patients experience suboptimal treatment results or glucocorticoid resistance, which may lead to progression to end-stage renal disease, impacting prognosis [3]. Tacrolimus, a novel phosphatase inhibitor with potent immunosuppressive effects, has been gradually introduced into clinical practice to enhance treatment efficacy. Based on this, this study aims to analyze changes in liver and kidney function and lipid metabolism in RNS patients after different treatments.

2. Materials and methods

2.1. General information

This study was approved by the hospital's medical ethics committee, and informed consent was signed by the patients' families. Sample selection period: from January 2018 to January 2021, with a total of 64 cases, all of which were patients with refractory nephrotic syndrome (RNS). They were randomly divided into a control group (n = 32) and an observation group (n = 32) based on a random number table method. The age range in the control group was 20–60 years, with an average age of 40.04 ± 3.12 years; the duration of illness ranged from 1 to 6 years, with an average of 3.41 ± 0.30 years; the body mass index (BMI) ranged from 18 to 24 kg/m², with an average of 21.48 ± 1.03 kg/m²; the gender ratio was 18 males and 14 females. The observation group had an age range of 21–60 years, with an average age of 40.08 ± 3.14 years; the duration of illness ranged from 1 to 7 years, with an average of 3.43 ± 0.32 years; BMI ranged from 18 to 24 kg/m², with an average of 21.46 ± 1.02 kg/m²; and a gender ratio of 16 males and 16 females. A comparison of these demographic data showed no statistically significant differences ($P > 0.05$), allowing for normal inter-group comparisons in the study.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Patients clinically diagnosed with RNS who met the relevant content of the "Expert Consensus on Immunosuppressive Therapy for Adult Nephrotic Syndrome in China" [4]; (2) Those with stable conditions and vital signs; (3) Those who had not received immunosuppressive therapy prior to enrollment.

Exclusion criteria: (1) Patients with mental disorders affecting normal communication; (2) Patients with allergic reactions to the study drugs; (3) Patients with immune-related diseases.

2.3. Methods

Control group: Intravenous infusion of 800 mg/m² of cyclophosphamide for injection mixed with 250 mL of sodium chloride injection, once a month; oral prednisone acetate tablets at a dose of 0.5–1.0 mg/kg/day, once daily.

Observation group: Tacrolimus capsules at a dose of 0.05–0.1 mg/kg/day, administered twice daily; oral prednisone acetate tablets were administered as in the control group. Both groups received treatment for six months.

2.4. Observation indicators

(1) Clinical efficacy: The overall clinical efficacy rate in both groups after six months of treatment was evaluated according to the standards in the "Expert Consensus on Immunosuppressive Therapy for Adult Nephrotic Syndrome in China" [4], including significant effect, effective, and ineffective. These criteria are described as follows: disappearance of relevant clinical symptoms and return of laboratory

indicators to normal; significant improvement in relevant clinical symptoms and laboratory indicators; and no change in relevant clinical symptoms and laboratory indicators after treatment.

(2) Liver function indicators: Fasting venous blood was collected before and six months after treatment in both groups, with a collection volume of 6 mL. Blood samples were centrifuged at 4°C for 10 minutes (3,500 rpm) to extract serum. Of this, 2 mL of serum was used to measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and albumin (ALB) levels by double-antibody sandwich enzyme-linked immunosorbent assay at the above time points.

(3) Kidney function indicators: The remaining 2 mL of serum was used to measure serum urea nitrogen (BUN) and serum creatinine (SCr) levels in both groups before and six months after treatment using an enzyme-coupled rate method. Additionally, 24-hour urine samples were collected from patients before and six months after treatment, and a PF-100 automatic biochemical analyzer (Shenzhen Pukang Electronics Co., Ltd.) was used to detect 24-hour urine protein quantification (24-hour UTP).

(4) Glucose and lipid metabolism: The remaining 2 mL of serum was analyzed with an automatic biochemical analyzer to measure serum triglyceride (TG) and cholesterol (TC) levels in both groups before and six months after treatment. Fasting fingertip blood (about 2 mL) was collected at the above time points, and a glucometer (model: HGM-121) produced by Suzhou Erda Medical Equipment Co., Ltd. was used to measure fasting blood glucose (FBG) levels in both groups.

2.5. Statistical analysis

SPSS 26.0 was used for data analysis in this study, with $P < 0.05$ as the threshold for statistically significant differences. Measurement data and count data are presented as (mean ± standard deviation) and [*n* (%)], respectively, and *t*-tests and χ^2 tests were used for analysis.

3. Results

3.1. Comparison of clinical efficacy between the two groups after six months of treatment

Table 1 compares the total clinical efficacy rate of the control and observation groups after six months of treatment, showing that the observation group had a significantly higher efficacy rate ($P < 0.05$), indicating a statistically significant difference as calculated by statistical software.

Table 1. Comparison of clinical efficacy after six months of treatment in the two groups [*n* (%)]

Group	*n*	Significant effect	Effective	Ineffective	Total effectiveness
Control	32	9 (28.13)	15 (46.88)	8 (25.00)	24 (75.00)
Observation	32	13 (40.63)	17 (53.13)	2 (6.25)	30 (93.75)
χ^2					4.267
P					0.039

3.2. Comparison of liver function indicators before and after six months of treatment in the two groups

Table 2 compares liver function indicators in the control and observation groups before and six months after treatment. Results show that after six months of treatment, serum ALT and AST levels in both groups decreased

compared to pre-treatment levels, with the observation group showing lower levels than the control group. Serum ALB levels increased, with the observation group showing higher levels than the control group. The differences were statistically significant ($P < 0.05$).

Table 2. Comparison of liver function indicators before and after six months of treatment in the two groups (mean ± SD)

Group	*n*	ALT (U/L)		AST (U/L)		ALB (ng/mL)	
		Before	After	Before	After	Before	After
Control	32	56.25 ± 9.40	46.81 ± 7.53*	78.88 ± 9.86	52.17 ± 7.39*	29.10 ± 3.15	34.47 ± 2.81*
Observation	32	55.96 ± 9.05	43.30 ± 4.07*	77.92 ± 9.81	44.48 ± 5.17*	30.16 ± 3.08	38.61 ± 2.26*
t		0.126	2.320	0.390	4.823	1.361	6.494
P		0.900	0.024	0.698	< 0.001	0.178	< 0.001

*Note: $P < 0.05$ compared to pre-treatment

3.3. Comparison of kidney function indicators before and after six months of treatment in the two groups

Table 3 compares kidney function indicators in the control and observation groups before and after six months of treatment. Results indicate that serum BUN, SCr, and 24-hour UTP levels decreased in both groups after six months of treatment compared to pre-treatment levels, with the observation group showing lower levels than the control group. These differences were statistically significant ($P < 0.05$).

Table 3. Comparison of kidney function indicators before and after six months of treatment in the two groups (mean ± SD)

Group	*n*	BUN (mmol/L)		SCr (μmol/L)		24-hour UTP (g)	
		Before	After	Before	After	Before	After
Control	32	10.13 ± 1.01	8.38 ± 1.11*	106.18 ± 10.04	90.68 ± 9.31*	4.08 ± 1.04	1.66 ± 0.32*
Observation	32	10.06 ± 1.05	6.07 ± 1.02*	105.94 ± 10.06	81.11 ± 8.18*	4.15 ± 1.01	0.79 ± 0.07*
t		0.272	8.668	0.096	4.368	0.273	15.024
P		0.787	< 0.001	0.924	< 0.001	0.786	< 0.001

*Note: $P < 0.05$ compared to pre-treatment

3.4. Comparison of glucose and lipid metabolism indicators before and after six months of treatment in the two groups

Table 4 compares glucose and lipid metabolism indicators in the control and observation groups before and after six months of treatment. Results show that serum TG and TC levels decreased in both groups after six months of treatment compared to pre-treatment levels, with the observation group showing lower levels than the control group, indicating a statistically significant difference ($P < 0.05$). FBG levels showed no significant difference before and after treatment in both groups ($P > 0.05$).

Table 4. Comparison of glucose and lipid metabolism indicators before and after six months of treatment in the two groups (mean ± SD, mmol/L)

Group	*n*	TG		TC		FBG	
		Before	After	Before	After	Before	After
Control	32	5.73 ± 1.07	4.02 ± 1.31*	7.28 ± 1.17	5.31 ± 1.04*	5.08 ± 1.11	4.96 ± 1.02*
Observation	32	5.61 ± 1.09	2.57 ± 0.76*	7.21 ± 1.15	3.42 ± 1.02*	5.01 ± 1.15	4.89 ± 1.06*
t		0.444	5.416	0.241	7.339	0.248	0.269
P		0.658	< 0.001	0.810	< 0.001	0.805	0.789

*Note: $P < 0.05$ compared to pre-treatment

4. Discussion

The incidence of refractory nephrotic syndrome in clinical practice continues to show a significant upward trend. The kidneys, being vital organs, are at risk of severe complications if patients do not receive timely and effective treatment, potentially endangering their lives. Currently, cytotoxic drugs combined with glucocorticoids are commonly used in clinical treatment, which can alleviate patients' symptoms to some extent; however, the associated toxic side effects limit their clinical efficacy [5,6].

Tacrolimus is a neurocalcin inhibitor with strong immunosuppressive properties and relatively mild drug toxicity. In previous studies, it was mainly used for liver disease treatment. Nowadays, tacrolimus has been found to not only provide immunosuppression but also effectively inhibit platelet aggregation and reduce inflammatory responses, making it widely used in the treatment of refractory nephrotic syndrome [7]. The results of this study indicate that, after six months of treatment, the total clinical efficacy rate in the observation group was significantly higher than in the control group. Additionally, the observation group showed lower serum ALT and AST levels and higher serum ALB levels compared to the control group after six months of treatment. This suggests that tacrolimus combined with glucocorticoids can reduce liver function damage in patients with refractory nephrotic syndrome and improve clinical efficacy, consistent with findings by Ding in clinical practice [8].

Analyzing these findings, the following explanation emerges: in patients with refractory nephrotic syndrome, the disease severity often leads to substantial proteinuria, causing a decrease in plasma colloid osmotic pressure and significant protein loss from the liver, which in turn impairs liver function and leads to abnormal serum ALT, AST, and ALB levels. When tacrolimus enters the body, it can effectively inhibit T lymphocyte proliferation, offering strong immunosuppressive effects, while being metabolized by the liver's cytochrome enzyme P-450-3A4 isoenzyme, thereby reducing liver damage. Furthermore, tacrolimus does not exhibit bone marrow suppression, allowing it to bind with endogenous cell receptors in the cytoplasm and form complexes that, in conjunction with glucocorticoids, enhance therapeutic efficacy [9,10].

The study results also show that serum BUN, SCr, 24 h UTP, TG, and TC levels in the observation group were lower than in the control group after six months of treatment, with no significant difference in FBG levels. This suggests that tacrolimus combined with glucocorticoids can effectively improve kidney function and lipid metabolism in patients with refractory nephrotic syndrome without affecting blood glucose levels, which is consistent with the findings of Deng *et al.* [11]. Analyzing this, the following explanation is derived: serum BUN,

SCr, and 24 h UTP are commonly used clinical markers of kidney function damage, while serum TG and TC are primary indicators of blood lipid metabolism, all of which can be used to assess the severity of refractory nephrotic syndrome. Treatment with tacrolimus and glucocorticoids can directly act on relevant effector cells and induce the liver enzyme system to effectively inhibit transcription factor dephosphorylation, thereby improving kidney function and regulating blood lipid metabolism [12].

5. Conclusion

In summary, tacrolimus combined with glucocorticoids in patients with refractory nephrotic syndrome can significantly reduce liver function damage, improve kidney function and blood lipid metabolism, and enhance clinical treatment efficacy.

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Disclosure statement

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References

[1] Guo HL, Li L, Xu ZY, et al., 2021, Steroid-resistant Nephrotic Syndrome in Children: A Mini-review on Genetic Mechanisms, Predictive Biomarkers and Pharmacotherapy Strategies. Curr Pharm Des, 27(2): 319–329. https://doi.org/10.2174/1381612826666201102104412

[2] Jiang N, 2022, Clinical Observation of Prednisone Combined with Cyclophosphamide Pulse Therapy for Refractory Nephrotic Syndrome. Guide of China Medicine, 20(36): 76–78.

[3] Qiu LR, Zhang RJ, Liao LP, 2023, Observation of the Clinical Effects of Tacrolimus Combined with Glucocorticoids in the Treatment of Refractory Nephrotic Syndrome. Medical Theory and Practice, 36(6): 979–981.

[4] Expert Group on Immunosuppressive Therapy for Adult Nephrotic Syndrome in China, 2014, Expert Consensus on Immunosuppressive Therapy for Adult Nephrotic Syndrome in China. Chinese Journal of Nephrology, 30(6): 467–474.

[5] Zhang DL, Luo L, Zheng LR, et al., 2020, Rituximab Should Not be Used as A Salvage Therapy for Secondary Refractory Nephrotic Syndrome. Chinese General Practice, 23(36): 4645–4650.

[6] Ni JY, Zhai WS, Li L, et al., 2022, Clinical Efficacy of Sequential Therapy with Yiqi Huayu Qingre Formula Based on Hormone Combined with Cyclophosphamide for Children with Refractory Nephrotic Syndrome. China Journal of Traditional Chinese Medicine and Pharmacy, 37(12): 7521–7525.

[7] Chen JT, 2019, Experiences on the Application Value of Tacrolimus and Glucocorticoids in Refractory Nephrotic Syndrome. Guide of China Medicine, 17(35): 73–74.

[8] Ding W, 2021, Analysis of Clinical Efficacy and Incidence of Adverse Reactions in Tacrolimus Combined with Glucocorticoids for the Treatment of Refractory Nephrotic Syndrome. Chinese Journal of Modern Drug Application,

15(6): 178–180.

[9] Zhang D, 2020, Clinical Observation of Tacrolimus Combined with Glucocorticoids in the Treatment of Refractory Nephrotic Syndrome. Chinese Journal of Modern Drug Application, 14(10): 139–141.

[10] Tan HJ, 2021, Clinical Efficacy and Safety of Tacrolimus Combined with Glucocorticoids in the Treatment of Refractory Nephrotic Syndrome. Journal of Clinical Rational Drug Use, 14(23): 95–96.

[11] Deng DY, Xu L, Liu K, 2021, Effects of Tacrolimus Capsules Combined with Glucocorticoids on Liver and Kidney Function, Glucose, and Lipid Metabolism in Patients with Refractory Nephrotic Syndrome. Journal of Clinical Rational Drug Use, 14(32): 112–114.

[12] Liu ZG, Liu YY, Chai FX, et al., 2020, Experience on the Clinical Value of Tacrolimus + Glucocorticoids in the Treatment of Nephrotic Syndrome. Journal of Aerospace Medicine, 31(5): 526–527.