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Original Research Article

Effect of combined use of prednisone and immunosuppressive therapy in patients with systemic lupus erythematosus, and its influence on incidence of adverse reactions

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Abstract

Purpose: *To study the effect of combined use of prednisone and immunosuppressive therapy for systemic lupus erythematosus (SLE), and its impact on the incidence of adverse reactions.*
Methods: *In total, 90 SLE patients treated in Longhui People's Hospital between January 2019 and January 2020 were included in this study, and assigned to receive either prednisone (control group) or immunosuppressive therapy and prednisone (study group) via the sealed envelope method. Outcome measures include immunoglobulin measured by enzyme-linked immunosorbent assay (ELISA), complement component 3 (C3) and C4 determined by immunoturbidimetric method, inflammatory factors such as INF-α, IL-10, and IL-6 levels, and the incidence of drug reactions.*
Results: *After treatment, the treatment group had higher levels of immunoglobulin indices and C3 and C4 levels than the control group ($p < 0.05$). There were lower serum inflammatory factor levels in the treatment group than in the control group ($p < 0.05$). Prednisone and immunosuppressive therapy resulted in higher treatment effectiveness and lower SLEDAI scores, versus prednisone alone ($p < 0.05$).*
Conclusion: *Prednisone and immunosuppressive therapy for SLE is safe, enhances treatment effectiveness, and improves clinical indicators in the patients. However, further trials are required prior to its application in clinical practice*

Keywords: *Systemic lupus erythematosus, Prednisone, Immunosuppressive therapy*

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease that occurs in women of childbearing age [1,2]. It occurs mostly in females, with the highest incidence in the age range of 20 - 40 years. The clinical manifestations of the disease are arthralgia, pericarditis, and decreased hemoglobin levels. Lupus mesenteric vasculitis and renal failure may easily occur if SLE is not properly managed, thereby seriously jeopardizing the lives of

patients [3-5]. The pathogenesis of SLE is still unclear. However, it is thought to be related to sex hormones and immunogenetics [6,7].

At present, the mainstay treatment strategy for the disease is drug therapy which is aimed at reducing the clinical symptoms of SLE in patients and maintaining a normal quality of life. However, to date, there is no known radical cure for the disease: symptoms are only relieved with scientific treatment [8]. Sole treatment with prednisone produces unsatisfactory results, which do not meet expected clinical outcomes [9]. Studies have revealed that the incorporation of immunosuppressive therapy effectively improved treatment results in patients. Therefore, the current study was carried out to assess the therapeutic effect of prednisone plus immunosuppressive therapy for SLE.

METHODS

General patient information

A total of SLE 90 patients treated in Longhui People's Hospital between January 2019 and January 2020 were included and assigned to a control group or a treatment group via the sealed envelope method.

Inclusion criteria

Patients who met the diagnostic criteria of SLE, who were confirmed via immunological examination and biochemical testing, and who did not use immunosuppressive agents 3 months prior to the study were included.

Exclusion criteria

Patients with other types of rheumatic diseases, with drug allergies, and during pregnancy or lactation were excluded from the study.

Ethics approval and consent

This study was approved by the ethics committee of Longhui People's Hospital (approval no. 2018-12-28), and performed according to international guidelines on human studies. The patients provided signed informed consent.

Treatments

The control group received 40 - 60 mg prednisolone tablets (Zhejiang Xianju Pharmaceutical Co. Ltd (Zhejiang, China); National approval no. H33021207), once a day. The dose was gradually decreased as the patient's condition improved. In addition to prednisolone, patients in the experimental group received immunosuppressive therapy with intravenous cyclophosphamide (Jiangsu Shengdi Pharmaceutical Co. Ltd; National Medicine Standard H32026196; specification: 0.5 g) at doses of 500 – 1000 mg/m^2, in addition to normal saline (20 - 30 mL) once a week, 2 times in a row. After an interval of 1 to 2 weeks, the treatment was repeated. The duration of treatment was 4 months.

Evaluation of parameters/indices

Serum immunoglobulins

Early morning fasting cubital venous blood was collected from each patient. The blood was centrifuged to obtain the serum, which was kept at -80 ℃. Enzyme-linked immunosorbent assay (ELISA) was used to determine pre- and post-treatment levels of serum IgA, IgG, and IgM. All operations were performed strictly in accordance with the instructions in ELISA kit.

Complement components 3 and 4

Fasting venous blood was obtained from the patients, and serum samples obtained after centrifugation were kept in a refrigerator at -20℃ prior to use in assay of complement component C3 and C4, using the immunoturbidimetric method. The assays were completed within 24 h, and all operations were strictly performed in accordance with the protocols indicated in assay kits purchased from Shanghai Luzhen Industrial Co. Ltd. (Shanghai, China).

Serum levels of INF-α, IL-10, and IL-6

Early morning fasting cubital venous blood samples collected from all subjects were centrifuged, and the sera were preserved at -80°C prior to use in the assay of serum INF-α, IL-10, and IL-6 levels using kits from Absen Biotech Co. Ltd. (Shenzhen, China).

Incidence of adverse reactions

The incidence of drug reactions such as liver damage, leukopenia, gastrointestinal reactions, and hair loss was recorded.

Treatment effectiveness

Treatment efficacy was considered markedly effective if the physical signs and urine protein of the patients returned to normal. Treatment was deemed effective if the patient's physical signs were mitigated, urine protein was decreased by more than 50 %. Treatment was deemed

ineffective if the patient's clinical symptoms did not change, or if they aggravated. The SLEDAI Rating Scale [10] was used to assess the severity of conditions of patients before and after treatment. The severity was assessed on a 4-Likert scale, with a score of 0-4 for basically no activity, 5-9 for mild activity, 10 -14 for moderate activity, and ≥ 15 for heavy activity.

Statistical analysis

Data analysis was done with SPSS 20.0 software, while GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to plot the graphics. Enumeration data were analyzed using χ^2 test, while measurement data were analyzed with *t*-test and normality test. Statistically significant differences were defined at $p < 0.05$.

RESULTS

General patient profile

The patient characteristics of the two groups, such as gender, average age, BMI, mean disease course, SAS score, SDS score, and place of residence were comparable ($p > 0.05$, Table 1).

Immunoglobulin levels

The treatment group had higher post-treatment immunoglobulin indexes levels than the control group ($p < 0.05$). (Table 2).

Complement levels

Table 3 shows that higher levels of C3 and C4 in the treatment group after treatment than the control group ($p < 0.05$).

Serum inflammatory factor indices

Prednisone plus immunosuppressive therapy resulted in lower serum levels of proinflammatory cytokines versus prednisone alone ($p < 0.05$; Table 4).

Table 1: Comparison of general information between the two groups of patients

Variable	Study group (n=45)	Control group (n=45)	χ^2	*P*-value
Gender			0.124	0.725
Male	5（11.11）	4（8.89）		
Female	40（88.89）	41（91.11）		
Mean age（years）	32.25±3.32	32.33±3.29	0.115	0.909
BMI（kg/m^2）	26.27±1.59	25.89±1.63	1.119	0.266
Mean course of disease (month)	30.21±2.17	30.25±2.15	0.088	0.930
SAS score	35.22±2.31	35.23±2.27	0.041	0.967
SDS score	45.15±2.31	45.17±2.29	0.041	0.967
Place of residence			0.050	0.822
Township	31(68.89)	30(66.67)		
Rural area	14(31.11)	15(33.33)		

Table 2: Comparison of immunoglobulin indexes between the two groups (mean ± SD, n = 45)

Group	IgA（g/L）		IgG（g/L）		IgM（g/L）	
	Before treatment	*After treatment*	*Before treatment*	*After treatment*	*Before treatment*	*After treatment*
Study	3.49±0.49	2.27±0.28	19.56±1.27	11.33±0.25	2.58±0.21	1.58±0.14
Control	3.51±0.52	3.21±0.35	19.55±1.28	14.89±0.38	2.57±0.22	2.21±0.23
t	0.188	14.068	0.037	52.502	0.220	15.696
P-value	0.852	＜0.001	0.970	＜0.001	0.826	＜0.001

Table 3: Comparison of complement level indicators between the two groups (mean ± SD, n = 45)

Group	C_3（mg/L）		C_4（mg/L）	
	Before treatment	*After treatment*	*Before treatment*	*After treatment*
Study	0.39±0.04	0.98±0.07	0.11±0.13	0.42±0.15
Control	0.40±0.03	0.61±0.05	0.12±0.14	0.17±0.13
t	1.342	28.853	0.351	8.449
P-value	0.183	＜0.001	0.726	＜0.001

Table 4: Comparison of serum inflammatory factor indexes between the two groups (mean ± SD, n = 45)

Group	INF-α（p/ng·L）		IL-10（p/ng·L）		IL-6（p/ng·L）	
	Before treatment	***After treatment***	***Before treatment***	***After treatment***	***Before treatment***	***After treatment***
Study	5.11±1.07	0.41±0.59	69.88±2.85	37.25±1.89	40.66±9.11	13.39±6.15
Control	5.08±1.05	3.51±0.79	69.75±2.84	55.88±1.91	40.65±9.12	25.15±7.11
t	0.134	21.091	0.217	46.509	0.005	8.932
P-value	0.894	＜0.001	0.829	＜0.001	0.996	＜0.001

Table 5: Comparison of the incidence of drug toxicity between the two groups {n（%, N = 45}

Group	Liver damage	Leukopenia	Gastrointestinal reaction	Hair loss	Total incidence
Study	2.22% (1/45)	4.44%（2/45）	2.22%（1/45）	0.00% (0/45)	8.89% (4/45)
Control	4.44% (2/45)	8.89%（4/45）	4.44%（2/45）	4.44% (2/45)	22.22% (10/45)
λ^2					3.045
P-value					0.081

Table 6: Comparison of clinical efficacy between the two groups [n（%, N = 45]

Group	Markedly effective	Effective	Ineffective	Total incidence
Study	68.89 % (31/45)	26.67%（12/45）	4.44%（2/45）	95.56%（43/45）
Control	44.44%（20/45）	24.44%（11/45）	31.11%（14/45）	68.89%（31/45）
λ^2				10.946
P-value				0.032

Incidence of adverse reactions

The differences in the incidence of adverse reactions between the two groups did not come up to the statistical standard *(p* > 0.05; Table 5).

Treatment efficacy

Patients receiving combined therapy of prednisone plus immunosuppressive therapy showed higher treatment efficacy and lower SLEDAI scores versus prednisone alone The SLEDAI scores of patients in the treatment group before and after treatment were 17.88 ± 1.25 and 4.11 ± 0.85 points, respectively, while SLEDAI scores of the control group before and after treatment were 17.85 ± 1.29 and 10.27 ± 1.05 points; respectively. (*p* < 0.05; Table 6 and Figure 2).

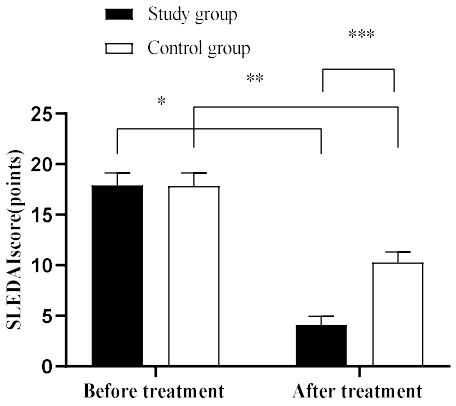

Figure 1: Comparison of SLEDAI scores between the two groups (mean ± SD). ***Note:*** **P* < 0.001, SLEDAI score of patients in the experimental group before treatment vs SLEDAI score after treatment; ***p* < 0.001, SLEDAI scores of the control group before treatment vs SLEDAI scores after treatment; ****p* < 0.001, SLEDAI scores between the two groups of patients after treatment

DISCUSSION

Currently, not much is known about the pathogenesis of SLE. However, some researchers are of the view that the disease is related to abnormal immune cell activation and abnormal hormone secretion [11]. Under the influence of different factors, SLE leads to decreases in T lymphocytes and decreases in the function of T suppressor cells, thereby increasing the incidence of lupus nephritis and other diseases [12].

The clinical treatment of SLE is based mainly on drugs, and prednisone, a glucocorticoid drug with a wide range of clinical applications, enhances protein decomposition and reduces glucose utilization, thereby elevating liver glycogen and blood sugar [13]. In addition, the drug inhibits the proliferation of connective tissue, controls the permeability of cell membranes, and reduces severe exudation, thereby suppressing the immune response and reducing the inflammatory

response. However, it has been clinically found that the therapeutic effect of prednisone when used as a single drug, is poor, while the addition of immunosuppressive therapy effectively improves clinical efficacy [14,15].

Cyclophosphamide, a clinically potent immunosuppressant, acts as an anti-inflammatory agent by effectively blocking the release of cytokines. Immunoglobulin index refers to immune protein components extracted from healthy plasma and purified and formulated through a series of processes [16]. The use of prednisone in combination with immune-suppressive therapy for SLE patients boosts immunity thereby improving the patient's conditions. Interestingly, the present study showed lower post-treatment immunoglobulin indexes in the study group, indicating that prednisone plus immunosuppressive therapy effectively improved the clinical indexes of patients and enhanced their recovery from the disease.

In addition, the clinical significance of C3 is similar to that of C4, and they are frequently present in infectious diseases. Excessive complement consumption increases the incidence of SLE. The current study found higher levels of C3 and C4 in the treatment group after treatment, indicating that the use of combined treatment with prednisone and immune-suppressive therapy effectively improved the conditions of the patients. Inflammatory factor indicators not only measure the degree of disease in SLE patients but also reflect clinical treatment efficacy. The results of this study demonstrated that the treatment group had lower serum levels of pro-inflammatory factors, indicating that prednisone plus immune-suppressive agents effectively mitigated the inflammatory responses in patients. Interestingly, both methods produced good effects. Moreover, the treatment group had lower SLEDAI scores, indicating that this treatment method produced promising results while ensuring safety, which is in concordance with the results of a previous study [17]. It was also shown that butylphthalide soft capsules and modified tonic exercise therapy yielded promising results [18].

CONCLUSION

This study has demonstrated that the use of prednisone and immunosuppressive therapy in SLE patients is a boon in terms of boosting treatment effect and enhancing clinical indices of patients, with a high safety profile.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

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.

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