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Original Article

Clinical efficacy and short-term prognosis of belimumab in the treatment of systemic lupus erythematosus in children

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Abstract: Objective: To evaluate the clinical efficacy and short-term prognosis of belimumab in treating pediatric systemic lupus erythematosus (SLE). Methods: A retrospective analysis was conducted on 208 pediatric patients with SLE who were admitted to our hospital between June 2019 and May 2023. Patients who received conventional glucocorticoid (GCs) treatment were assigned to the control group (n=118), while those who received GCs combined with belimumab were assigned to the observation group (n=90). Results: The observation group exhibited a higher total effective rate, faster symptom improvement, and a lower SLEDAI-2K score (all $P<0.05$). After 24 weeks of treatment, the observation group showed lower levels of antinuclear antibody (ANA), anti-double-stranded DNA (ds-DNA) antibody, antinucleosome (AnuA), immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and 24-hour urine protein (all $P<0.05$). Meanwhile, levels of complement C3, complement C4, white blood cell count, hemoglobin, and platelet count were higher (all $P<0.05$). The average daily reduction in GCs dosage was greater in the observation group ($P<0.05$). No significant difference in adverse reactions was observed between the two groups ($P>0.05$). The observation group had a lower cumulative recurrence rate within 6 months ($P<0.05$). A decrease in ANA levels was identified as an independent protective factor against SLE recurrence (OR=0.860, $P<0.05$). Conclusions: Conventional glucocorticoid therapy combined with belimumab effectively enhances treatment outcomes in pediatric SLE patients, reduces the risk of short-term recurrence, and does not increase adverse reactions.

Keywords: Children, systemic lupus erythematosus, glucocorticoids, immunosuppressive agents, belimumab, efficacy and prognosis

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the formation of pathogenic autoantibodies and immune complexes, which mediate organ and tissue damage [1]. Childhood SLE refers to the onset of SLE before the age of 18 years, accounting for 15% to 20% of all cases [2]. Compared with adult SLE, childhood SLE tends to be more active and aggressive, with a higher likelihood of kidney, blood, and central nervous system involvement, more severe organ damage, and a worse prognosis [3]. The pathogenesis of SLE remains unclear, and no specific treatment is available. Glucocorticoids (GCs) have potent anti-inflammatory, anti-allergic, and immunosuppressive effects, making them the cornerstone of SLE treatment [4, 5]. However, GCs use can lead to dependence or drug resistance in some children, and prolonged use may result in serious adverse effects such as osteoporosis, osteonecrosis, growth restriction, infections, and metabolic disorders [6].

In recent years, biologic agents have offered new therapeutic possibilities for SLE. Belimumab, a humanized monoclonal antibody that specifically inhibits B lymphocyte stimulator (BLyS), blocks its binding to B cell receptors, reducing the survival and differentiation of autoreactive B cells and decreasing autoantibody levels [7, 8]. Belimumab has been approved by both the National Medical Products

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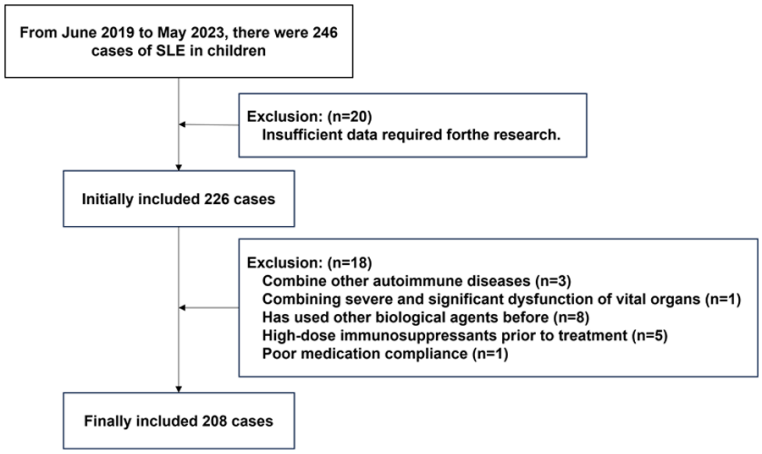

Figure 1. Flowchart of patient screening process. SLE: systemic lupus erythematosus.

Administration of China and the U.S. Food and Drug Administration for the treatment of pediatric SLE in children aged 5 and older [9]. It is currently the only biologic agent approved for this age group. Compared with traditional immunosuppressants, belimumab offers the advantages of targeted action and high safety. However, its efficacy, optimal dosing regimen, and organ-protective effects in children with SLE still require further investigation. Research on belimumab's use for pediatric SLE is still limited. This study, therefore, focuses on childhood SLE and examines the applicability and advantages of belimumab compared to conventional GCs therapy, with the aim of providing a reference for pediatric SLE treatment, optimizing clinical decision-making, and promoting the rational use of biologics in this population.

Materials and methods

Study design and patients

This study is a retrospective cohort study. A total of 208 children with SLE who were treated at Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, from June 2019 to May 2023 were consecutively included through the hospital's electronic medical record system. Based on the treatment methods, children who received conventional GCs therapy were assigned to the control group (n=118), and children treated with belimumab in addition to conventional GCs therapy were assigned to the observation group (n=90).

The detailed patient inclusion process is illustrated in **Figure 1**.

Inclusion criteria: (1) Age <18 years; (2) Fulfillment of the 2012 International Systemic Lupus Erythematosus Classification Criteria [10] and clinical diagnosis of SLE; (3) Availability of complete data for analysis.

Exclusion criteria: (1) Presence of other autoimmune diseases; (2) Severe dysfunction of major organs (e.g., heart, liver, kidneys); (3) Presence of other serious infectious diseases; (4) Previous use of belimumab or other biologic agents; (5) Use of belimumab less than three times or poor compliance (e.g., frequent discontinuation of treatment) in the observation group; (6) Prior use of excessive doses of immunosuppressive agents.

Sample size calculation: Based on previous literature and pre-test results, the expected total effective rate of treatment in the control group is 80% (P_1), and in the observation group, it is 95% (P_2). With the average effective rate of treatment, $P=(P_1 + P_2)/2$, with $\alpha=0.05$ and $1-\beta=0.8$, and accounting for a 20% loss to follow-up, it was calculated that at least 75 cases are required per group. The calculation formula is as follows:

$$n = \frac{\left(Z_{\alpha\text{-}2}\sqrt{2P(1-P)} + Z_{\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right)^2}{(P_1-P_2)^2}$$

This study was approved by the Ethics Committee of Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China.

Treatment methods

Both groups received general treatments, including gastric mucosa protection, calcium and potassium supplementation, anti-infection therapy, and symptomatic support.

Control group: Prednisolone acetate (250 mg) + 0.9% sodium chloride (250 mL) intravenous infusion for 3 days, followed by oral predniso-

Table 1. Comparison of baseline data

Information	Control group (n=118)	Observation group (n=90)	t/χ^2	*P*
Age (years, $\bar{x} \pm s$)	11.06±2.91	11.11±3.74	0.109	0.914
Gender [n (%)]			<0.001	0.983
Male	29 (24.58)	22 (24.44)		
Female	89 (75.42)	68 (75.56)		
BMI (kg/m^2, $\bar{x} \pm s$)	19.59±2.13	20.07±1.39	1.937	0.054
Duration (months, $\bar{x} \pm s$)	3.30±1.01	3.47±0.99	1.218	0.225
Severe clinical symptoms [n (%)]				
Skin and mucous membrane damage	31 (26.27)	27 (30.00)	0.353	0.552
Renal involvement	52 (44.07)	41 (45.56)	0.046	0.831
Nervous system involvement	22 (18.64)	15 (16.67)	0.137	0.712
Thrombosis	18 (15.25)	16 (17.78)	0.238	0.626
Thrombocytopenia	17 (14.41)	20 (22.22)	2.133	0.144

BMI: body mass index.

lone (0.5-1 mg/kg/d in the morning), gradually tapered according to clinical condition. Mycophenolate mofetil was administered at a dose of 20-30 mg/kg/d, divided into two oral doses. Tacrolimus was given at a dose of 0.05-0.15 mg/kg/d, divided into two oral doses. Cyclophosphamide (400 mg) + 0.9% sodium chloride (250 mL) intravenous infusion was given once a month.

Observation group: Treatment was the same as the control group, but with the addition of belimumab (10 mg/kg) + 0.9% sodium chloride injection, diluted to 250 mL by intravenous infusion. Belimumab was administered every 2 weeks initially, and then every 4 weeks after the third dose. Both groups were treated for at least 24 weeks. The treatment plan was determined by the attending physician based on the child's condition and guideline recommendations, and the guardian was informed.

Data extraction

Clinical data were collected from the hospital's electronic medical record system.

Baseline data: Age, gender, body mass index (BMI), disease duration, organ involvement.

Efficacy indicators: Disease activity, symptom improvement time, immunological indicators, inflammatory markers, blood/urine test results, glucocorticoid dosage.

Safety data: Adverse reactions, recurrence rate.

Outcome measures

Primary efficacy indicators: Total effective rate of treatment [11]: The total clinical effective rate was compared between the two groups after 24 weeks of treatment.

Marked effect: Complete disappearance of clinical symptoms and normalization of immune markers (e.g., antibodies, complement, immunoglobulin).

Effective: Effective symptom relief, improvement of immunological markers by one-third or more, no deterioration of other inflammatory or blood/urinary system markers.

Invalid: Not meeting the above criteria.

The total effective rate = (markedly effective cases + effective cases)/total cases × 100%.

Disease activity: The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) [12] was compared between the two groups before treatment and at the 4th, 12th, and 24th weeks of treatment. The total score ranges from 0 to 105: 0-4 points: No activity; 5-9 points: Mild activity; 10-14 points: Moderate activity; ≥15 points: Severe activity.

Immune function: Immune markers were compared before treatment and after 24 weeks,

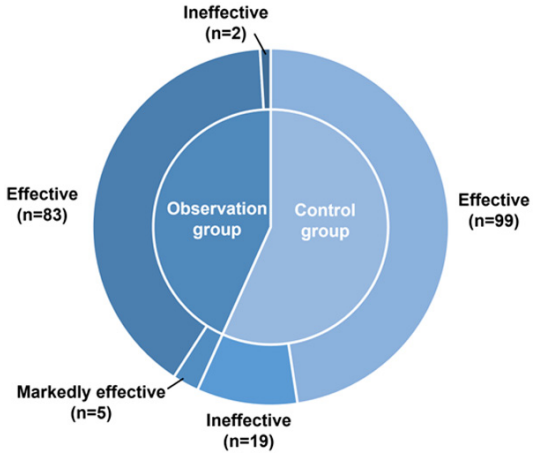

Figure 2. Analysis of the overall therapeutic effects of the two groups of treatments.

including antinuclear antibody (ANA), anti-double-stranded DNA (dsDNA) antibody, anti-nucleosome (AnuA), immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), complement C3, and complement C4. Blood samples (5 mL) were collected in the morning, with ANA quantified by indirect immunofluorescence, anti-dsDNA antibodies by enzyme-linked immunosorbent assay (ELISA), AnuA by immunoimprinting, and IgA, IgG, IgM, C3, and C4 by turbidimetry.

Secondary efficacy indicators: Symptom improvement time: Time for skin lesion alleviation, reduction in proteinuria, pain relief, and body temperature normalization was compared.

Inflammatory markers: Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were compared before and after 24 weeks. ESR was measured by the Westergren method, and CRP by immunoturbidimetry.

Blood/Urine test indicators: White blood cell count, red blood cell count, hemoglobin, platelet count, neutrophil and lymphocyte percentages, and 24-hour urinary protein quantification were compared before and after 24 weeks. Routine blood tests were performed using an automatic blood cell analyzer. Urine samples (5 mL) were collected, and 24-hour urinary protein was measured by immunoscattering.

Glucocorticoid dosage: The reduction in the average daily dose of prednisolone at the 4th, 8th, 12th, 16th, 20th, and 24th weeks was compared. The reduction amplitude = (baseline daily dose - weekly daily dose)/baseline daily dose × 100%.

Safety indicators: Adverse reactions: The incidence of adverse reactions during treatment was compared between groups, including infusion reactions, hypersensitivity, infections, abnormal blood glucose, gastrointestinal ulcers, etc.

Recurrence rate: Recurrence rates within 6 months of further treatment were tracked through hospital records and follow-up information. Criteria for SLE relapse included: (1) Disease activity resurgence: A SLEDAI-2K score increase of ≥4 points. (2) Deterioration of laboratory indicators: For example, significant decrease in complement C3/C4 levels. (3) Organ damage progression: Confirmed by imaging. (4) Treatment failure: Need for restarting treatment or increasing glucocorticoids or immunosuppressants.

Statistical analysis

SPSS 26.0 software was used for statistical analysis. Quantitative data with normal distribution were expressed as mean ± standard deviation ($\bar{x}\pm s$). Paired sample t-tests were used for intra-group comparisons, and independent sample t-tests were used between groups. Data not following a normal distribution were expressed as median and interquartile range [M (Q_{25}, Q_{75})], and Wilcoxon rank-sum tests were used. Qualitative data were expressed as number of cases and percentage [n (%)], with chi-square tests. Repeated measures analysis of variance (ANOVA) was used for multiple time-point comparisons, corrected using the Bonferroni test. Kaplan-Meier analysis and Log-rank tests were used to compare cumulative recurrence rates between the two groups. Binary logistic regression was used to identify prognostic factors for SLE. Receiver operating characteristic (ROC) curves were used to evaluate the clinical value of influencing factors. $P<0.05$ was considered statistically significant.

Results

Comparison of baseline data

There were no significant differences in age, gender, BMI, disease duration, daily predni-

Table 2. Comparison of the improvement time of the main symptoms

	Skin lesion relief (d)	Proteinuria reduction (w)	Pain relief (d)	Temperature drop (d)
Control group (n=118)	8.94±2.76	3.46±0.61	8.25±2.23	4.64±0.93
Observation group (n=90)	6.51±2.32	2.21±0.44	5.26±1.29	2.41±0.67
t	6.897	17.193	12.145	20.145
P	<0.001	<0.001	<0.001	<0.001

d: day; w: week.

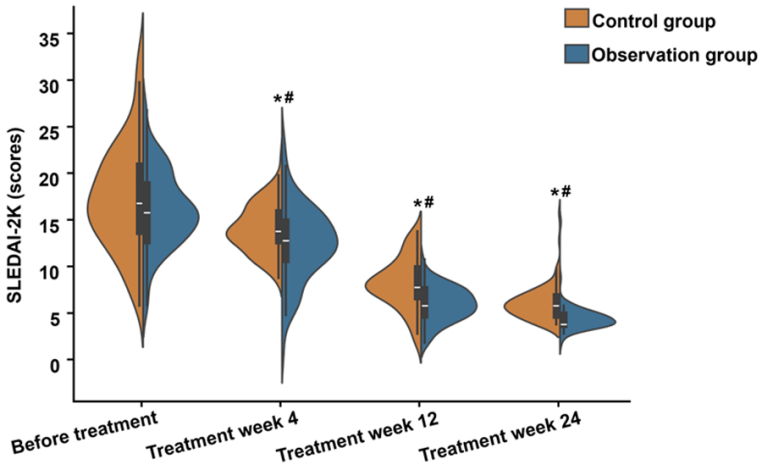

Figure 3. Comparison of disease activity between the two groups at different time points. SLEDAI-2K: Systemic lupus erythematosus disease activity index; Compared to before treatment, **P*<0.05; Compared with the control group, #*P*<0.05.

sone dosage, or clinical symptoms of inflammation between the two groups (all *P*>0.05), as shown in **Table 1**.

Comparison of the total effective rate

The total effective rate in the control group was 83.90% (99/118), compared to 97.78% (88/90) in the observation group. The observation group showed a significantly higher effective rate than the control group (χ^2=10.836, *P*<0.05), as shown in **Figure 2**.

Improvement time of main symptoms

At the 24th week of treatment, the time for skin lesion relief, reduction in proteinuria, pain relief, and body temperature drop in the observation group was significantly shorter than in the control group (all *P*<0.05), as shown in **Table 2**.

Comparison of disease activity

At 4th, 12th, and 24th weeks of treatment, the SLEDAI-2K median was significantly lower in the observation group compared to the control group (all *P*<0.05). Both groups showed a downward trend in SLEDAI-2K over time. The main effect of the groups was significant (F_{group}=18.623, *P*<0.001), as was the main effect of time (F_{time}=226.554, *P*<0.001), with a significant interaction effect ($F_{group\cdot time}$=11.561, *P*<0.001). See **Figure 3**.

Comparison of immune function

After 24th weeks of treatment, levels of ANA, anti-dsDNA, AnuA, IgA, IgG, and IgM were significantly decreased, while complement C3 and C4 were significantly increased in both groups (all P<0.05). The levels of ANA, anti-dsDNA, AnuA, IgA, IgG, and IgM were significantly lower, and complement C3 and C4 were significantly higher in the observation group compared to the control group (all *P<0.*05), as shown in **Table 3**.

Comparison of inflammatory markers

At the 24th week of treatment, the levels of ESR and CRP decreased significantly in both groups (both *P*<0.05). The levels of ESR and CRP in the observation group were significantly lower than in the control group (both *P*<0.05). See **Figure 4**.

Comparison of blood/urine test indicators

At the 24th week of treatment, the white blood cell count, red blood cell count, hemoglobin, platelet count, and lymphocyte percentage were significantly increased in both groups, while neutrophil percentage and 24-hour urine protein quantification decreased significantly

Table 3. Comparison of immune function indexes between the two groups

Immune function indicators	Control group (n=118)	Observation group (n=90)	*t/Z*	*P*
ANA (kU/L, $\bar{x} \pm s$)				
Before treatment	144.88±37.27	144.93±27.83	0.011	0.991
Week 24th of treatment	26.07±8.62	10.00±3.20	18.636	<0.001
T	34.258	46.089		
P	<0.001	<0.001		
anti-dsDNA (kU/L, $\bar{x} \pm s$)				
Before treatment	212.15±42.95	216.46±38.41	0.751	0.453
Week 24th of treatment	47.71±10.14	8.87±2.02	40.541	<0.001
T	42.034	51.153		
P	<0.001	<0.001		
AnuA (U/mL, $\bar{x} \pm s$)				
Before treatment	53.51±4.52	52.77±3.94	1.226	0.221
Week 24th of treatment	11.53±3.37	6.58±1.90	12.497	<0.001
T	83.052	105.497		
P	<0.001	<0.001		
IgA (g/L, $\bar{x} \pm s$)				
Before treatment	3.48±0.73	3.50±0.72	0.225	0.822
Week 24th of treatment	2.94±0.31	2.51±0.54	6.701	<0.001
T	7.613	10.158		
P	<0.001	<0.001		
IgG (g/L, $\bar{x} \pm s$)				
Before treatment	21.88±3.82	21.48±4.49	0.697	0.486
Week 24th of treatment	15.40±2.36	12.32±3.29	7.536	<0.001
T	15.524	17.204		
P	<0.001	<0.001		
IgM (g/L, $\bar{x} \pm s$)				
Before treatment	2.86±0.58	2.98±0.48	1.640	0.103
Week 24th of treatment	1.81±0.32	1.47±0.23	8.679	<0.001
T	14.288	26.266		
P	<0.001	<0.001		
Complement C3 [g/L, [M(Q_{25}, Q_{75})]				
Before treatment	0.4 (0.4, 0.5)	0.5 (0.4, 0.5)	1.259	0.208
Week 24th of treatment	1 (0.9, 1.2)	1.2 (1, 1.32)	3.379	0.001
Z	21.002	22.829		
P	<0.001	<0.001		
Complement C4 [g/L, [M (Q_{25}, Q_{75})]				
Before treatment	0.2 (0.1, 0.2)	0.2 (0.1, 0.2)	1.304	0.192
Week 24th of treatment	0.4 (0.3, 0.4)	0.5 (0.4, 0.5)	6.625	<0.001
Z	19.802	21.549		
P	<0.001	<0.001		

ANA: antinuclear antibody; anti-dsDNA: anti-double-stranded DNA; AnuA: Anti-nucleosome; IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M.

(all $P<0.05$). The white blood cell count, hemoglobin, and platelet count in the observation group were significantly higher, and the 24-hour urine protein quantification was significantly

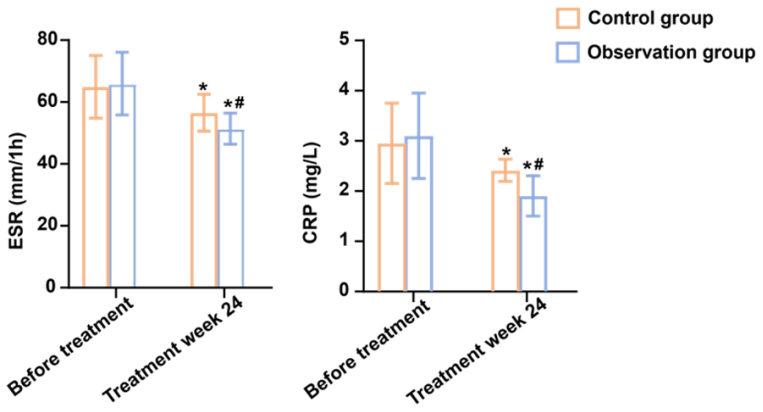

Figure 4. Comparison of inflammatory markers between the two groups. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; Compared to before treatment, *P<0.05; Compared with the control group, #P<0.05.

lower than in the control group (all P<0.05), as shown in **Table 4**.

Comparison of hormone dosage

With the extension of treatment, the daily dosage of prednisolone gradually decreased in both groups (all P<0.05). At the 4th, 8th, 12th, 16th, 20th, and 24th weeks, the average daily dose reduction in the observation group was significantly higher than in the control group (all P<0.05). The reduction in the average daily dose of prednisolone showed an upward trend with time. The main effect of the groups was significant (F_{group}=333.28, P<0.001), as was the main effect of time (F_{time}=280.81, P<0.001), with a significant interaction effect ($F_{group\text{-}time}$=22.614, P<0.001). See **Figure 5**.

Comparison of adverse reactions

The most common adverse reaction in the control group was gastrointestinal ulcer, while in the observation group, it was infusion reaction. The overall incidence of adverse reactions was 12.71% in the control group and 11.11% in the observation group, with no statistically significant difference (P>0.05). See **Table 5**.

Comparison of SLE recurrence

In the control group, 12 cases had disease recurrence, with a recurrence rate of 10.17%, and an average recurrence-free survival time of 5.713 months. In the observation group, 2 cases had recurrence, with a recurrence rate of 2.22%, and an average recurrence-free survival time of 5.966 months, as shown in **Figure 6**. The cumulative recurrence rate in the observation group was significantly lower than in the control group (Log-rank χ^2=9.372, P=0.009).

Analysis of influencing factors on the prognosis of SLE

Baseline data and indicators at the 24th week were compared. The non-recurrence group had significantly lower levels of SLEDAI-2K, ANA, anti-dsDNA antibodies, IgA, and 24-hour urine protein, while levels of hemoglobin and neutrophils were higher compared to the recurrence group (all P<0.05), as shown in **Table 6**. Binary logistic regression analysis was conducted to assess the factors influencing SLE prognosis. The assignment is shown in **Table 7**. This analysis revealed that a decrease in ANA levels was an independent protective factor for non-recurrence (P<0.05), as shown in **Table 8**. ROC curve analysis showed that the area under the curve (AUC) of ANA for predicting SLE recurrence was 0.835, as shown in **Figure 7**.

Discussion

Clinically, SLE is generally considered to be closely linked to environmental factors, genetic predisposition, and endocrine disorders, particularly involving estrogen. Under the combined influence of these factors, the body experiences a reduction in T lymphocyte count, accompanied by enhanced B lymphocyte proliferation, ultimately impairing T cell function. Pathologically, SLE is primarily characterized by immune complex deposition [13]. In clinical practice, the core principle of SLE management is to regulate immune function.

GCs are steroid hormones secreted by the zona fasciculata of the adrenal cortex, with their synthesis and secretion regulated by adrenocorticotropic hormone. Upon binding to glucocorticoid receptors (GRs), GCs induce conformational changes in GRs, which then regulate various physiological processes, including immunity, metabolism, and osmotic pressure [14]. However, monotherapy with GCs has drawbacks

Table 4. Comparison of blood/urine test indicators between the two groups

Blood/Urine test indicators	Control group (n=118)	Observation group (n=90)	*t*	*P*
White blood cells ($\times10^9$/L, $\bar{x} \pm s$)				
Before treatment	3.59±1.60	3.54±1.54	0.217	0.828
Week 24 of treatment	6.06±1.33	7.45±1.41	7.281	<0.001
T	12.970	17.080		
P	<0.001	<0.001		
Red blood cells ($\times10^{12}$/L, $\bar{x} \pm s$)				
Before treatment	3.661.07	3.65±1.13	0.101	0.920
Week 24 of treatment	4.08±1.19	4.18±1.11	0.665	0.507
T	3.032	3.289		
P	0.003	0.001		
Hemoglobin (g/L, $\bar{x} \pm s$)				
Before treatment	91.87±7.19	89.13±14.18	1.676	0.096
Week 24 of treatment	116.09±5.67	122.81±8.97	6.222	<0.001
T	29.231	19.276		
P	<0.001	<0.001		
Platelets ($\times10^9$/L, $\bar{x} \pm s$)				
Before treatment	116.31±39.95	114.31±35.15	0.375	0.708
Week 24 of treatment	269.51±45.81	297.68±56.56	3.856	<0.001
T	27.047	26.724		
P	<0.001	<0.001		
Neutrophils (%, $\bar{x} \pm s$)				
Before treatment	67.85±9.84	66.63±9.79	0.883	0.378
Week 24 of treatment	61.19±7.72	58.88±10.29	1.788	0.076
T	5.500	5.125		
P	<0.001	<0.001		
Lymphocytes (%, $\bar{x} \pm s$)				
Before treatment	21.62±5.83	20.61±5.83	1.235	0.218
Week 24 of treatment	28.16±5.12	28.96±5.87	1.039	0.300
T	8.982	10.317		
P	<0.001	<0.001		
24-hour urinary protein quantification (g, $\bar{x} \pm s$)				
Before treatment	4.73±1.31	4.73±1.47	0.013	0.990
Week 24 of treatment	3.06±1.06	2.62±1.08	2.883	0.004
T	10.604	11.368		
P	<0.001	<0.001		

such as prolonged administration cycles and high dosage requirements, which can lead to increased long-term toxicities, tissue damage, and a higher risk of drug resistance [15].

Modern approaches to SLE treatment prioritize disease control through personalized regimens, stepwise therapeutic strategies, combination therapies, and non-pharmacological interventions. These approaches aim to minimize cumulative GCs dosage, optimize treatment outcomes, and reduce adverse effects.

Recent years have seen extensive research on BLyS inhibitors to enhance therapeutic efficacy. BLyS is a 285-amino acid type II transmembrane protein predominantly expressed on T cells, dendritic cells, and monocytes. It can be

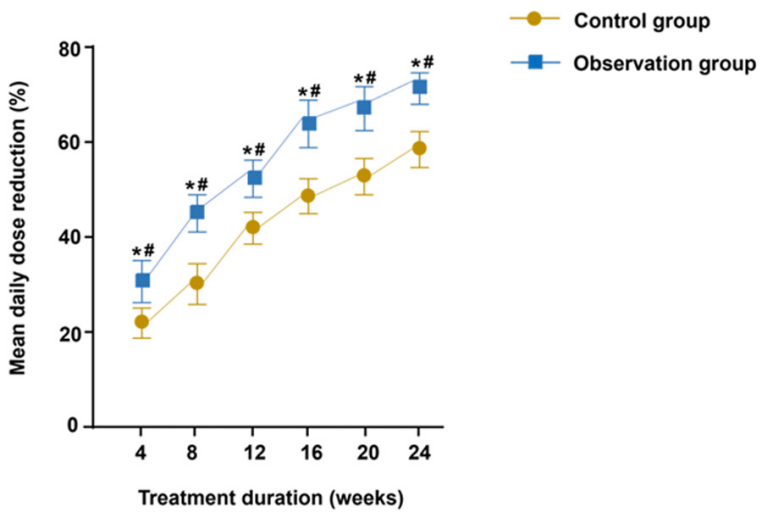

Figure 5. Comparison of hormone dosage between the two groups at different time points. Compared to before treatment, $^{*}P<0.05$; Compared with the control group, $^{\#}P<0.05$.

secreted into circulation as soluble molecules, regulating B cell pool dynamics by promoting B cell proliferation, survival, and immunoglobulin repertoire maturation during B cell development-key processes in autoimmune pathogenesis [16, 17]. Pathogenic overexpression of BLyS in SLE patients makes it a prime therapeutic target. Belimumab, a BLyS-specific inhibitor, binds soluble BLyS to prevent receptor engagement, thereby arresting B cell maturation, desensitizing B cells to immune stimuli, and selectively depleting autoreactive B cell clones through apoptosis induction [18].

Our study, evaluating belimumab adjunctive therapy alongside standard GCs treatment in pediatric SLE, demonstrated significantly reduced autoantibody (ANA, anti-dsDNA, AnuA) and immunoglobulin (IgA, IgG, IgM) levels in the treatment group at 24 weeks compared to controls. Belimumab's targeted inhibition of B cell differentiation prevents immune complex-mediated tissue damage. Furthermore, the treatment group showed elevated complement C3 and C4 levels, mechanistically explained by belimumab's suppression of B cell activation, reducing autoantibody production and immune complex formation, thereby mitigating classical complement pathway overactivation and decreasing complement consumption [19, 20]. These findings align with previous reports by Kang et al. [21], Wang et al. [22], and Li et al. [23], further validating BLyS inhibition as an effective therapeutic strategy.

The observation group demonstrated significantly improved inflammatory markers post-treatment, with lower ESR and CRP levels compared to controls. This improvement can be attributed to two mechanisms: reduced immune complex formation, which diminished complement activation and endothelial cell stimulation, leading to decreased monocyte/macrophage chemotaxis and neutrophil infiltration, and B-cell function inhibition, which downregulated pro-inflammatory cytokines (IL-6, TNF-α), suppressed hepatic CRP production, and enhanced erythrocyte aggregation properties [24]. Hematologic and renal parameters also showed marked improvement, with elevated hemoglobin and platelet counts, along with reduced 24-hour proteinuria. These multisystem improvements reflect belimumab's organ-protective effects, corroborated by Elshaer et al.'s meta-analysis of 593 pediatric SLE cases demonstrating consistent benefits in hematology and nephrology [25]. These therapeutic benefits stem from decreased pathogenic autoantibodies mitigating hematopoietic damage, attenuated complement-mediated inflammation preserving bone marrow microenvironments, and notable nephroprotection through reduced glomerular immune complex deposition, which diminished proteinuria and improved erythropoiesis and iron utilization [26-28].

The safety of belimumab 10 mg/kg in children with SLE has been consistent with its known safety profile in adults, with no allergic reactions or systemic imbalances following infusion [29-31]. A study reported that 20% of children in the belimumab group experienced mild infections, which improved with symptomatic treatment, while no serious infections or other adverse events were observed. In contrast, the control group, treated with prednisone and traditional immunosuppressants, had an adverse event rate of 32% [21]. This study found no sig-

Table 5. Comparison of incidence of adverse reactions between the two groups [n (%)]

	Infusion reactions	Hypersensitivity reaction	Infection	Abnormal blood glucose	Gastrointestinal ulcers	Total
Control group (n=118)	2 (1.69)	3 (2.54)	2 (1.69)	3 (2.54)	5 (4.24)	15 (12.71)
Observation group (n=90)	5 (5.56)	1 (1.11)	0	2 (2.22)	2 (2.22)	10 (11.11)
χ^2	1.303	0.589	2.282	0.022	0.665	0.124
P	0.243	0.635	0.507	>0.999	0.701	0.725

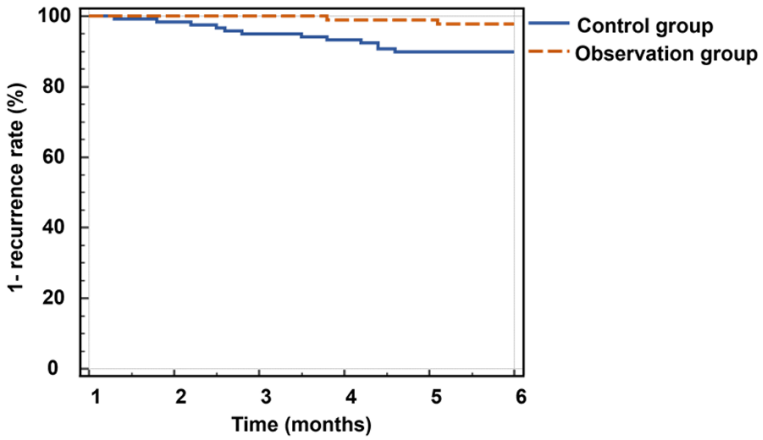

Figure 6. Kaplan-Meier analysis of recurrence in the two groups.

nificant difference in the overall incidence of respiratory tract infections between the two groups. Infusion reactions in the observation group were manageable with pretreatment and standardized procedures, confirming the safety of belimumab combined with conventional therapy.

An important finding in this study was the significantly greater reduction in hormone dosage in the observation group compared to the control group, coupled with a significantly reduced recurrence rate. Previous studies have shown that belimumab reduces the amount of hormone needed and facilitates earlier clinical remission [32, 33]. This suggests that combined therapy enhances therapeutic effects by continuously inhibiting the BLyS pathway, reducing the expansion of self-reactive B cell clones. The recovery of T cell function improves immune tolerance and inhibits the initiation of abnormal immune responses. Early control of multi-system damage prevents the chronic tissue damage cycle, creating favorable conditions for hormone reduction. The combined immunomodulatory effects lower the risk of recurrence and improve long-term prognosis, while also reducing reliance on long-term GCs therapy and minimizing the risk of adverse effects.

Binary logistic regression analysis showed that a decrease in ANA levels was an independent protective factor for non-recurrence of SLE. ROC curve analysis also demonstrated that ANA is a reliable predictor of SLE recurrence in children. This emphasizes the importance of dynamic monitoring of ANA titers in the management of childhood SLE, as changes in ANA levels may reflect the intensity of the body's autoimmune response and help predict the risk of recurrence. However, some studies have pointed out that ANA detection alone lacks high sensitivity and specificity for SLE and should be combined with other antibody tests for comprehensive assessment [34].

This study has several limitations. It is a retrospective single-center study with a small sample size and short follow-up duration, which may affect the reliability of the results and the evaluation of long-term efficacy, and introduces potential selection bias. Additionally, the study primarily relied on routine clinical indicators to assess efficacy, lacking deeper biomarker analysis and patient-reported outcomes, such as quality of life. Furthermore, the relatively homogenous study population limits the generalizability of the results to other racial groups. These limitations highlight the need for multicenter prospective studies with larger sample sizes and longer follow-up periods, incorporating more comprehensive efficacy evaluation indicators.

Table 6. Univariate analysis of the non-relapse group and the relapse group of SLE

	Non-recurrence group (n=194)	Recurrence group (n=14)	$t/\chi^2/Z$	P
Age (years, $\bar{x} \pm s$)	11.13±3.33	10.36±2.65	0.853	0.394
Gender [n (%)]			<0.001	>0.999
Male	48 (24.74)	3 (21.43)		
Female	146 (75.26)	11 (78.57)		
BMI (kg/m^2, $\bar{x} \pm s$)	19.85±1.88	19.16±1.37	1.343	0.181
Duration (months, $\bar{x} \pm s$)	3.39±1.01	3.14±0.77	1.116	0.280
Severe clinical symptoms [n (%)]				
Skin and mucous membrane damage	54 (27.84)	4 (28.57)	<0.001	>0.999
Renal involvement	90 (46.39)	3 (21.43)	3.292	0.070
Nervous system involvement	36 (18.56)	1 (7.14)	0.514	0.474
Thrombosis	31 (15.98)	2 (14.29)	<0.001	>0.999
Thrombocytopenia	35 (18.04)	2 (14.29)	<0.001	>0.999
SLEDAI-2K [scores, M (Q_{25}, Q_{75})]	5.00 (4.00, 6.00)	6.00 (5.00, 7.00)	2.246	0.025
ANA [kU/L, M (Q_{25}, Q_{75})]	16.00 (9.98, 26.05)	39.95 (31.23, 42.58)	4.184	<0.001
anti-dsDNA [kU/L, M (Q_{25}, Q_{75})]	34.40 (9.00, 49.50)	45.85 (39.43, 53.00)	1.996	0.046
AnuA [U/mL, M (Q_{25}, Q_{75})]	8.70 (12.23, 6.50)	10.10 (7.30, 12.93)	0.878	0.380
IgA (g/L, $\bar{x} \pm s$)	2.74±0.48	3.02±0.26	2.207	0.028
IgG (g/L, $\bar{x} \pm s$)	14.07±3.21	14.02±2.93	0.053	0.958
IgM (g/L, $\bar{x} \pm s$)	1.68±0.38	1.84±0.40	1.478	0.141
Complement C3 (g/L, $\bar{x} \pm s$)	1.11±0.26	1.00±0.28	1.441	0.151
Complement C4 (g/L, $\bar{x} \pm s$)	0.41±0.09	0.40±0.08	0.297	0.766
ESR (mm/1 h, $\bar{x} \pm s$)	54.09±6.10	56.99±5.75	1.721	0.087
CRP (mg/L, $\bar{x} \pm s$)	2.18±0.40	2.38±0.31	1.819	0.070
White blood cells ($\times 10^9$/L, $\bar{x} \pm s$)	6.68±1.51	6.52±1.76	0.364	0.716
Red blood cells ($\times 10^{12}$/L, $\bar{x} \pm s$)	4.12±1.69	4.19±0.97	0.216	0.829
Hemoglobin (g/L, $\bar{x} \pm s$)	119.41±7.95	113.36±6.52	2.780	0.006
Platelets ($\times 10^9$/L, $\bar{x} \pm s$)	283.44±52.33	257.50±51.07	1.794	0.074
Neutrophils (%, $\bar{x} \pm s$)	60.53±9.13	55.50±4.27	3.820	0.001
Lymphocytes (%, $\bar{x} \pm s$)	28.56±5.55	27.79±4.25	0.509	0.611
24-hour urinary protein quantification (g, $\bar{x} \pm s$)	2.81±1.06	3.67±1.17	2.908	0.004

BMI: body mass index; SLEDAI-2K: Systemic lupus erythematosus disease activity index; ANA: antinuclear antibody; anti-dsDNA: anti-double-stranded DNA; AnuA: Anti-nucleosome; IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

In conclusion, this study explored the efficacy of belimumab combined with conventional GCs-based therapy for childhood SLE. The results demonstrate that this combination not only curbs autoantibody production but also regulates the complement system, providing synergistic organ protection, particularly for the blood and kidneys. This treatment approach improves clinical symptoms, reduces disease activity, and lowers recurrence rates, offering a promising strategy for individualized treatment of childhood SLE. Moreover, monitoring ANA levels can aid in predicting prognosis and guiding management. However, due to the study's

Table 7. Assignment case

Variable	Assignment
SLE recurred conditions	1 = recurrence, 2 = non-recurrence
SLEDAI-2K	original value input
ANA	original value input
anti-dsDNA	original value input
IgA	original value input
Hemoglobin	original value input
Neutrophils	original value input
24-hour urinary protein quantification	original value input

SLE: systemic lupus erythematosus; SLEDAI-2K: Systemic lupus erythematosus disease activity index; ANA: antinuclear antibody; anti-dsDNA: anti-double-stranded DNA; IgA: immunoglobulin A.

Table 8. Binary logistic regression analysis of prognosis of SLE

	β	*SE*	*Wald* χ^2	*P*	*OR*	*95% CI*
SLEDAI-2K	-0.250	0.177	2.006	0.157	0.779	0.551-1.001
ANA	-0.151	0.044	11.818	<0.001	0.860	0.789-0.937
anti-dsDNA	0.032	0.030	1.085	0.298	1.032	0.973-1.096
IgA	-2.019	1.293	2.438	0.118	0.133	0.011-1.675
Hemoglobin	0.041	0.067	0.378	0.534	1.0419	0.914-1.188
Neutrophils	4.844	9.980	0.236	0.627	1.089	1.000-1.185
24-hour urinary protein quantification	-0.550	0.352	2.439	0.118	0.577	0.290-1.151

SLEDAI-2K: Systemic lupus erythematosus disease activity index; ANA: antinuclear antibody; nti-dsDNA: anti-double-stranded DNA; IgA: immunoglobulin A.

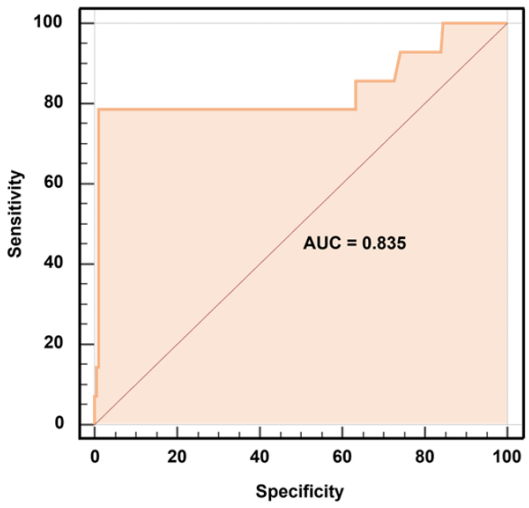

Figure 7. ROC curve analysis of ANA for predicting SLE recurrence. AUC: area under the ROC curve.

limitations, future prospective studies with larger sample sizes and longer follow-up are necessary for further validation.

Disclosure of conflict of interest

None.

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