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Peer Reviewer of *World Journal of Clinical Pediatrics*, Fateen Ata, MSc, MBBS, ABHS (Internal Medicine) Academic Editor, Academic Fellow, Academic Research, Doctor, Endocrinology, Hamad Medical Corporation, Qatar. docfateenata@gmail.com

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WJCP mainly publishes articles reporting research results and findings obtained in the field of pediatrics and covering a wide range of topics including anesthesiology, cardiology, endocrinology, gastroenterology, hematology, immunology, infections and infectious diseases, medical imaging, neonatology, nephrology, neurosurgery, nursing medicine, perinatology, pharmacology, respiratory medicine, and urology.

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Case Control Study

BCD020 rituximab bioanalog compared to standard treatment in juvenile systemic lupus erythematosus: The data of 12 months case-control study

Elvira Kalashnikova, Eugenia Isupova, Ekaterina Gaidar, Lyubov Sorokina, Maria Kaneva, Vera Masalova, Margarita Dubko, Tatiana Kornishina, Natalia Lubimova, Ekaterina Kuchinskaya, Irina Chikova, Rinat Raupov, Olga Kalashnikova, Mikhail Kostik

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Elvira Kalashnikova, Eugenia Isupova, Ekaterina Gaidar, Lyubov Sorokina, Maria Kaneva, Vera Masalova, Margarita Dubko, Tatiana Kornishina, Irina Chikova, Rinat Raupov, Olga Kalashnikova, Mikhail Kostik, Hospital Pediatrics Department, Saint-Petersburg State Pediatric Medical University, Saint-Petersburg 194100, Russia

Natalia Lubimova, Ekaterina Kuchinskaya, Mikhail Kostik, Research Laboratory of Autoimmune and Autoinflammatory Diseases, Almazov National Medical Research Centre, Saint Petersburg 197341, Russia

Rinat Raupov, Department of Rheumatology, Turner National Medical Research Center for Children's Orthopedics and Trauma Surgery, Saint-Petersburg 197136, Russia

Corresponding author: Mikhail Kostik, MD, PhD, Professor, Hospital Pediatrics, Saint-Petersburg State Pediatric Medical University, Lytovskaya 2, Saint-Petersburg 194100, Russia. kost-mikhail@yandex.ru

Abstract**BACKGROUND**

Systemic lupus erythematosus (SLE) is the most frequent and serious systemic connective tissue disease. Nowadays there is no clear guidance on its treatment in childhood. There are a lot of negative effects of standard-of-care treatment (SOCT), including steroid toxicity. Rituximab (RTX) is the biological B-lymphocyte-depleting agent suggested as a basic therapy in pediatric SLE.

AIM

To compare the benefits of RTX above SOCT.

METHODS

The data from case histories of 79 children from the Saint-Petersburg State Pediatric Medical University from 2012 to 2022 years, were analyzed. The diagnosis of SLE was established with SLICC criteria. We compared the outcomes of treatment of SLE in children treated with and without RTX. Laboratory data, doses of glucocorticosteroids, disease activity measured with SELENA-SLEDAI,

and organ damage were assessed at the time of initiation of therapy and one year later.

RESULTS

Patients, treated with RTX initially had a higher degree of disease activity with prevalence of central nervous system and kidney involvement, compared to patients with SOCT. One year later the disease characteristics became similar between groups with a more marked reduction of disease activity (SELENA-SLEDAI activity index) in the children who received RTX [-19 points (17; 23) since baseline] compared to children with SOCT [-10 (5; 15.5) points since baseline, $P = 0.001$], the number of patients with active lupus nephritis, and daily proteinuria. During RTX therapy, infectious diseases had three patients; one patient developed a bi-cytopenia.

CONCLUSION

RTX can be considered as the option in the treatment of severe forms of SLE, due to its ability to arrest disease activity compared to SOCT.

Key Words: Systemic lupus erythematosus; Children; Rituximab; Anti-B-cell therapy; Glucocorticosteroids

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Core Tip: Rituximab (RTX), known as an anti-B-cells agent, is actively discussed as one of the main drugs for severe systemic lupus erythematosus. Various studies have been conducted to evaluate its effectiveness, but their results are ambiguous. We show the benefits of RTX above the standard-of-care treatment in children.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is one of the most frequent systemic connective tissue diseases, which is characterized by an unpredictable course, affecting different organs and systems, often simultaneously[1,2]. Juvenile SLE has a more aggressive and severe course in children compared to adults, due to a higher frequency of kidney, central nervous system, and blood involvement[2-5]. Macrophage activation syndrome (MAS) is a difficult-to-recognize life-threatening complication of SLE, belonging to the family of hemophagocytic lymphohistiocytosis influencing the disease course and outcomes[6]. The disease severity and outcomes related to lupus nephritis (LN) occur in about 40% of patients, most often during the first 5 years from the onset of the disease[7-9]. Reduced damage to organs and systems, flare prevention, and improved quality of life of the patients are the main treatment goals of SLE[1,2]. Standard of care treatment (SOCT) for SLE includes glucocorticosteroids, hydroxychloroquine, and cytostatic drugs such as cyclophosphamide, cyclosporine A, methotrexate, azathioprine, mycophenolate mofetil (MMF) and usually associated with toxic side effects[2,4,5,10]. Despite the toxicity of glucocorticosteroids and the recommendations of the European Alliance of Associations for Rheumatology (EULAR) to minimize doses, there are no uniform schemes and rates of reduction of glucocorticosteroids, except for lupus nephritis[4,11]. The optimization of SLE treatment in children is necessary. The use of biological drugs makes it possible to achieve faster remission and reduce the toxic side effects of SOCT[12].

Rituximab (RTX) is one of the biologics used for the treatment of SLE. RTX is a chimeric mouse antibody directed against the CD20 antigen of B-lymphocytes. Depleting the pool of B-lymphocytes, RTX acts only on mature B-lymphocytes, without affecting stem and plasma cells[3]. RTX is proposed in some studies as an alternative or additional therapeutic approach for SLE[13-15]. In North America (United States, Mexico), Europe, and Australia, RTX is still used as an induction therapy for lupus nephritis off-label, despite the first successful reports in LN were published about 20 years ago[12,16]. The data about RTX efficacy in SLE are contradictory. RTX is still considered an off-label drug only if first-line therapy with cyclophosphamide or MMF fails, according to the EULAR2019 recommendations[17]. However, the position of using RTX as a starting therapy in combination with corticosteroids and non-biological disease-modifying antirheumatic drugs (DMARDs) remains open and requires more evidence of efficacy and safety[2,8,10,18,19].

Our study aimed to compare the safety and efficacy of RTX therapy in comparison with SOCT in children with systemic lupus erythematosus.

MATERIALS AND METHODS

Study design

A single-center retrospective cohort study included the data from the medical histories of 79 SLE children from 2012 to 2022.

Inclusion criteria

(1) The diagnosis of systemic lupus erythematosus in patients under 18 years of age was established according to the criteria of Systemic Lupus International Collaborating Clinic (SLICC) 2012[20]; and (2) patients were selected from the database if the data about at least 12 months of observation were available.

Exclusion criteria

Absence or incomplete information about the first 12-month course of the treatment.

Population and treatment arms

Nineteen children from the study group received RTX therapy in the first six months from the onset of the disease and were observed at least twelve months from the initiation of the RTX therapy. Sixty children received SOCT, which included glucocorticosteroid, hydroxychloroquine, non-biologic DMARDs, such as mycophenolate mofetil, cyclosporine, cyclophosphamide, and also were observed at least one year after the start of therapy.

Indications for the RTX were

(1) A highly active course of systemic lupus erythematosus with kidney and central nervous system involvement, including resistance to previous therapy; (2) a presence of a recurrent course of autoimmune hemolytic anemia or thrombocytopenia, requiring repeated doses of corticosteroids, replacement therapy (blood and platelet transfusion); and (3) a presence of signs of corticosteroid toxicity if it is impossible to reduce the dose of corticosteroids to 10 mg/d or 0.2 mg/kg/d, whichever is less.

RTX treatment protocol

RTX was prescribed at a dose of 375 mg/m² weekly, no more than 500 mg per infusion (2-4 infusions) with repeated courses every 6-12 months, depending on the degree of disease activity, the severity of B-cell depletion, the level of IgG. The decision about the treatment protocol was made by the group of the most experienced pediatric rheumatologists.

Assessments and outcomes

The assessment of the main characteristics of patients was carried out at the time of the initiation of RTX or SOCT, then after 12 ± 3 months from the start of therapy. At each time point, laboratory parameters were evaluated: complete blood cell, immunological tests - antinuclear antibodies (ANA), antibody against double-stained DNA (anti-dsDNA), complement level, assessment of urine protein excretion, presence of active lupus nephritis), the daily dose of glucocorticosteroids (GCS), the calculation of disease activity on the SELENA-SLEDAI scale, which allows to distinguish four degrees of disease activity: 0 points - no activity, 1-5 points - minimal activity, 6-10 points - moderate activity, 11-19 points - high activity, and > 20 points - very high activity[21]. MAS was diagnosed according to the previously published criteria by Parodi *et al*[22].

Methods of statistical data analysis

The analysis of the obtained data was carried out using the statistical software package Statistica v. 10.0 (StatSoft Inc., United States). Quantitative variables were assessed for compliance with normal distribution using the Kolmogorov-Smirnov test allows to use of nonparametric methods of analysis due to the absence of the normal distribution. The description of quantitative variables was expressed in the median and quartiles Me (Q1; Q3). The categorical variables were expressed in absolute numbers and parts (%). Comparison of two independent groups of quantitative variables was carried out using the Mann-Whitney test, categorical variables - using the Chi-square test, or Fisher's exact test, if the expected frequency was less than 5. Differences or relationships were considered statistically significant if $P < 0.05$.

RESULTS

Characteristics of the patients in the SLE onset

Patients, treated with RTX were older at the initial point of the study (baseline-start of the therapy), compared to patients from the SCOT group. They had frequently central nervous system involvement, hepatomegaly, lymphadenopathy, palmar erythema, proteinuria, decreased glomerular filtration rate (GFR), and higher SLEDAI (more patients with high activity, grade four) and higher frequency of using high-dose IV glucocorticosteroids. They also tended to more frequent development of pleurisy, and lupus nephritis. The incidence of MAS was also higher in the group of children treated with RTX. All cases of MAS developed during the disease onset. Early treatment with RTX allowed the use of fewer non-biologic DMARDs. The baseline characteristics of children from two groups are presented in Table 1.

Table 1 The characteristics of the patients at the time of the start of the treatment, *n* (%)

Parameter	Rituximab (<i>n</i> = 19)	SOCT (<i>n</i> = 60)	<i>P</i> value
Demography			
Sex, male	4 (21)	11 (18)	0.829
Onset age, years, Me (25%; 75%)	14 (12; 16)	12 (10; 14)	0.035
Clinical features			
Skin involvement	18 (95)	50 (83)	0.257
Oral mucosa involvement	8 (58)	16 (27)	0.203
Alopecia	3 (16)	16 (27)	0.334
Arthritis	15 (78)	42 (70)	0.449
Pleurisy	6 (32)	8 (12)	0.070
Pericarditis	5 (26)	8 (12)	0.184
Ascitis	3 (16)	3 (5)	0.122
Myocarditis	2 (11)	7 (12)	0.856
CNS involvement	9 (47)	13 (22)	0.030
Splenomegaly	5 (26)	12 (20)	0.560
Hepatomegaly	9 (47)	14 (23)	0.045
Lymphadenopathy	8 (42)	10 (17)	0.022
Lung involvement	3 (16)	3 (5)	0.122
Palmar erythema	5 (26)	5 (8)	0.040
Livedo	3 (16)	5 (8)	0.348
Fever	11 (58)	32 (53)	0.728
Trombosis	1 (5)	3 (5)	0.964
MAS	4 (21)	1 (2)	0.003
Renal involvement			
Nephritis	8 (42)	17 (28)	0.081
Kidney biopsy	3/8 (38)	7/17 (42)	0.670
Class of nephritis			
I	0 (0)	0 (0)	0.700
II	0 (0)	0 (0)	
III	1/3 (33)	3/7 (43)	
IV	2/3 (67)	3/7 (43)	
V	0 (0)	1/7 (14)	
Hematuria	8/8 (100)	17/17 (100)	0.124
Proteinuria	8/8 (100)	17/17 (100)	0.487
Proteinuria, g/L, Me (25%; 75%)	0,31 (0; 0,93)	0,1 (0,0; 0,3)	0.154
Proteinuria, g/24 h, Me (25%; 75%)	0,49 (0,12; 1,2)	0,17 (0,0; 0,3)	0.046
Urea, mmol/L, Me (25%; 75%)	5,8 (4,8; 9,6)	4,2 (3,5; 5,5)	0.003
Creatinine, mcmol/L, Me (25%; 75%)	58 (52; 94)	59 (54; 70)	0.856
GFR, mL/1.73/m ²	131 (72,0; 151)	130 (115; 147)	0.077
Decreased GFR	3 (16)	2 (3)	0.052
Dialysis	0 (0)	1 (2)	0.493
Laboratory features			

ANA-positivity	19 (100)	52 (87)	0.094
ANA level, titer, Me (25%; 75%)	1920 (1280; 5120)	2560 (640; 10240)	0.859
Anti-dsDNA antibodies	15 (79)	43 (72)	0.532
Anti-dsDNA, U/L (25%; 75%)	102 (12; 150)	63 (14; 237)	0.975
Positive Coombs	11/16 (69)	15/34 (44)	0.104
Low complement	11/14 (79)	15/30 (50)	0.073
Complement C3, g/L, Me (25%; 75%)	0.64 (0.35; 1.0)	0.84 (0.74; 0.94)	0.170
Complement C4, g/L, Me (25%; 75%)	0.1 (0.05; 0.17)	0.12 (0.1; 0.24)	0.610
Anaemia	12 (63)	31/59 (52.5)	0.418
Hemoglobine, g/L, Me (25%; 75%)	111 (98; 129)	111 (100; 126)	0.865
Thrombocytopenia	9 (47)	18 (30)	0.118
Platelets, 10 ⁹ /L, Me (25%; 75%)	232 (189; 285)	269 (178; 328)	0.454
Leucopenia	11 (58)	23 (38)	0.134
WBC, 10 ⁹ /L, Me (25%; 75%)	5.3 (4.2; 11.1)	5.4 (4.2; 8.3)	0.526
Lymphopenia	6 (33)	6 (10)	0.023
ESR, mm/h, Me (25%; 75%)	21 (8; 31)	18 (5; 37)	0.766
C-reactive protein (CRP), mg/L, Me (25%; 75%)	0.7 (0; 2.0)	1.0 (0.2; 3.7)	0.841
SLE activity			
SLEDAI onset score, Me (25; 75%)	22 (13; 26)	12 (9; 17)	0.002
SLEDAI onset, grade			0.005
0 grade	0 (0)	0 (0)	
I grade	0 (0)	5 (8)	
II grade	3 (16)	20 (33)	
III grade	5 (26)	25 (42)	
IV grade	11 (58)	10 (17)	
Treatment			
Intravenous corticosteroids	15 (79)	22 (37)	0.002
Corticosteroids, mg/kg, Me (25%; 75%)	1.0 (0.7; 1.0)	1.0 (0.4; 1.0)	0.854
Hydroxychloroquine	9 (47.4)	35/58 (60.3)	0.321
Non-biologic DMARDs	11 (58)	58 (97)	0.00001
Cyclophosphamide	5 (26)	23 (38)	0.340
Other DMARDs	6 (32)	37 (63)	0.054
Mycophenolate mofetil	2 (11)	20 (33)	0.630
Azathioprine	2 (11)	6 (10)	
Cyclosporine	0 (0)	2 (3)	
Methotrexat	2 (11)	9 (15)	

Anti-dsDNA: Antibody against double-stained DNA; ANA: Antinuclear antibodies; CNS: Central nervous system; DMARD: Disease-modifying anti-rheumatic drugs; ESR: Erythrocyte sedimentation rate; GFR: Glomerular filtration rate; MAS: Macrophage activation syndrome; Me: Median; SLEDAI: Systemic lupus erythematosus disease activity index; SOCT: Standard of care treatment; WBC: White blood cells.

Characteristics of the patients (outcomes) at the end of the study

At the end of the study, after twelve months, the disease characteristics between studied groups became equal, except for a tendency to higher levels of hemoglobin and lower part of patients having anti-dsDNA antibodies and low complement. Detailed characteristics of children at the end of the study are presented in [Table 2](#).

Table 2 Characteristics of the patients (outcomes) at the end of the study, *n* (%)

Parameter	RTX (<i>n</i> = 19)	SOCT (<i>n</i> = 60)	<i>P</i> value
Laboratory features			
ANA positivity	16 (84)	42 (70)	0.222
ANA level, titer, Me (25%; 75%)	640 (320; 2560)	640 (160; 2560)	0.849
Anti-dsDNA antibodies	3 (16)	26 (43)	0.079
Anti-dsDNA U/L (25%; 75%)	5.1 (0; 12.0)	7.4 (0.6; 57.4)	0.166
Low complement	3 (16)	25 (42)	0.098
Complement C3, g/L, Me (25%; 75%)	0.92 (0.8; 11)	1.07 (0.72; 1.4)	0.409
Complement C4, g/L, Me (25%; 75%)	0.19 (0.14; 0.27)	0.17 (0.12; 0.25)	0.594
Hemoglobine, g/L, Me (25%; 75%)	133 (127; 138)	124 (111; 133)	0.06
Platelets, 10 ⁹ /l, Me (25%; 75%)	276 (240; 306)	269 (215; 335)	0.712
WBC, 10 ⁹ /l, Me (25%; 75%)	4.9 (4.4; 5.8)	5.5 (4.5; 6.5)	0.252
ESR, mm/h, Me (25%; 75%)	6 (2; 20)	7 (2; 18)	0.365
SLE activity			
SLEDAI onset score, Me (25; 75%)	3 (0; 4)	2 (0; 4)	0.599
SLEDAI onset, grade			0.804
0 grade	6 (32)	16 (26)	
I grade	9 (47)	34 (57)	
II grade	4 (21)	9 (15)	
III grade	0 (0)	0 (0)	
IV grade	0 (0)	1 (2)	
Kidney involvement			
Hematuria	6/8 (75)	4/17 (24)	0.015
Proteinuria	1/8 (13)	2/17 (12)	0.958
Active nephritis	1/8 (13)	5/17 (29)	0.356
Proteinuria, g/L, Me (25%; 75%)	0.07 (0; 0.1)	0 (0; 0.07)	0.209
Proteinuria, g/24 h, Me (25%; 75%)	0.15 (0.02; 0.3)	0 (0; 0.16)	0.066
Urea, mmol/L, Me (25%; 75%)	3.7 (3.1; 4.4)	3.84 (3.05; 4.66)	0.526
Creatinine, mmol/L, Me (25%; 75%)	0.06 (0.05; 0.07)	0.06 (0.05; 0.07)	0.78
Treatment			
GCS, mg/kg, Me (25%; 75%)	0.1 (0.07; 0.15)	0.13 (0; 0.2)	0.569
Hydroxychloroquine	15 (78)	37 (62)	0.167
Mycophenolate mofetil	9 (47)	33 (55)	0.824
Azathioprine	2 (11)	4 (7)	
Cyclophosphamide	3 (16)	9 (15)	
Cyclosporine	0 (0)	2 (3)	
Methotrexate	1 (5)	7 (12)	

Anti-dsDNA: Antibody against double-stained DNA; ANA: Antinuclear antibodies; ESR: Erythrocyte sedimentation rate; GCS: Glucocorticosteroids; SLEDAI: Systemic lupus erythematosus disease activity index; WBC: White blood cells.

During the 12-month study period the more impressive reduction of the SLEDAI, the number of patients with active LN, and daily proteinuria were observed. Data are in [Table 3](#).

DISCUSSION

In our study, some benefits of RTX treatment for pediatric SLE were found. During the 12-month observation period, a more impressive reduction in disease activity and improvement in lupus nephritis was observed.

RTX has not received official approval either in adult or pediatric practice despite many years of experience in the treatment of systemic lupus erythematosus[8,10,17]. Numerous series of retrospective studies and published clinical cases have shown the effectiveness of RTX in patients with varying degrees of activity systemic lupus erythematosus, including forms with a catastrophic course, which, together with expert opinion, allowed to include RTX into the treatment algorithms for the of systemic lupus erythematosus both for children and adults[3,9,23].

Biological drugs, including RTX, are recommended for the treatment of SLE, but the study results are contradictory[24, 25]. Some randomized controlled trials showed improvement in blood tests (anti-dsDNA, normalization of complement levels of C3 and C4), without changes in the outcomes of the disease one year after the start of treatment[24]. In the largest randomized controlled trial the Lupus Nephritis Assessment with RTX study (LUNAR), there was no significant difference in achieving a complete response between patients receiving RTX and SOCT at the control time points, although the proportion of patients with a partial response was greater in patients, treated with RTX[24]. There was a significant improvement in serological markers of disease activity, such as a decrease in antibodies to DNA, an increase in complement levels, and a decrease in the degree of proteinuria in patients who received RTX, which was also noted in the non-randomized studies[3,10,25,26].

The results of the above-mentioned studies corresponded with our results: improvement of certain laboratory parameters has been achieved, but there is no statistically significant difference between the outcomes of the disease a year after the start of therapy. The analysis of various non-randomized studies from different countries of the world showed a positive effect of RTX in systemic lupus erythematosus in adults and children[3,5,10]. Reduction of the activity of the disease, increased hemoglobin level, decreasing ESR and levels of ANA and anti-dsDNA antibodies, and the part of children having cytopenia demonstrated in several studies[3,5,10,27]. RTX is effective for the treatment of lupus nephritis in children, whom increased C3 and C4 Levels, GFR, and serum albumin and decreased urine albumin/creatinine ratio and proteinuria and GCS dose detected[3,5,10,17,26-28]. Additionally, some studies reported a decrease in creatinine, but the data were statistically non-significant[17]. There is also conflicting data that the use of biological therapy for lupus nephritis did not lead to a decrease in the albumin-creatinine ratio[29]. A recent study on 14 pediatric LN showed the additional RTX therapy to conventional therapy improved proteinuria, eGFR, and serological markers. Three patients who required acute kidney replacement therapy became dialysis-free after RTX[30]. We found decreased activity and proteinuria in our study similar to previous. The absence of a significant effect in some randomized studies suggests to use of RTX not as a means of inducing remission, but as an auxiliary therapy in patients with SLE[31].

However, 27 studies demonstrated the positive effect of RTX in patients refractory to standard therapy, including cyclophosphamide and MMF[17]. The inclusion of patients with primary LN without preceding experience of cyclophosphamide or MMF in a large randomized LUNAR study did not show the superiority of RTX over non-biological DMARDs[24]. On the one hand, RTX has shown its effectiveness in patients who have not previously received any treatment, which does not allow us to evaluate the benefits of RTX in comparison with standard non-biological therapy. On the other hand, RTX was able to induce remission in cases where standard therapy with non-biological DMARDs failed and disease duration and treatment exposure were longer[17,32,33].

In our study, RTX was prescribed to children in the first year of the disease who had had a higher disease activity at the time of initiation of therapy. There was no statistically significant difference in the activity of SLE between the two groups at the end of the study, but at the same time, there was a more significant decrease in the activity of the disease in the RTX group. It allows us to conclude that RTX shows its effectiveness in a more severe course of the disease.

Limitations

Our study has limitations, related to retrospective study designs, initial differences between studied groups, missing data, and absence of a unique treatment protocol with administration and tapering of the drugs. Personal opinion about prescribing the RTX and all the abovementioned limitations may make the study results inaccurate and other-estimated.

CONCLUSION

RTX can be considered as the option in the treatment of severe forms of SLE, due to its ability to rapidly arrest the disease activity compared to SOCT. Faster and intensive reduction of the disease activity and better nephritis outcomes are the main benefits of RTX above the SOCT. Further pediatric randomized controlled trials are required to evaluate its efficacy and safety in comparison with standard therapy, with further consideration of the possible use of RTX as an induction therapy in children with high-moderate disease activity.

Table 3 Dynamics of the main indicators of the disease activity in studied groups

Reduction since the baseline of	Rituximab (n = 19)	SOCT (n = 60)	P value
Anti-dsDNA, U/L (25%; 75%)	-139.7 (106.4; 374.1)	-129.0 (81.0; 369.4)	0.75
Anti-dsDNA, U/L (25%; 75%)	-93.7 (93.1; 95.0)	-83.7 (63.2; 96.4)	0.29
SLEDAI, points	-19 (17; 23)	-10 (5.0; 15.5)	0.001
SLEDAI, %	86.9 (82.6; 100.0)	77.5 (60.0; 100.0)	0.147
Daily GCS dose, mg/kg	-0.8 (0.6; 0.9)	-0.57 (0.0; 1.0)	0.874
Daily GCS dose, %	-88 (85; 90)	-83.3 (66.7; 94.6)	0.525
Proteinuria, %	-96.7 (91.3; 100)	-100 (72.9; 100)	0.967
Daily proteinuria, g/24 h	-0.83 (0.27; 1.24)	-0.1 (0; 0.34)	0.031
Patients without active LN since BL, %	-7/8 (88)	-12/17 (71)	0.356

Anti-dsDNA: Antibody against double-stained DNA; BL: Baseline; GCS: Glucocorticosteroids; SLEDAI: Systemic lupus erythematosus disease activity index; LN: Lupus nephritis.

ARTICLE HIGHLIGHTS

Research background

Systemic lupus erythematosus (SLE) is a serious life-threatening disease. Systemic corticosteroids are the still basis of the treatment of SLE.

Research motivation

The side effects of corticosteroids required to change the treatment plans of SLE with biologic implementation.

Research objectives

The place of biologics in the treatment of SLE is not yet determined, despite a lot of clinical observations and studies.

Research methods

The comparison of 12-month course of treatment of pediatric SLE patients with rituximab (RTX) and standard of care treatment without RTX was done.

Research results

RTX worked effective in SLE patients with high activity with improvement of kidney disease.

Research conclusions

RTX might be added in the treatment protocol of the severe pediatric SLE.

Research perspectives

The following randomized controlled trials are required in pediatric SLE.

FOOTNOTES

Author contributions: Kostik M and Kalashnikova E contributed to conceptualization writing—original draft preparation, writing—review and editing; Kostik M and Chikova I contributed to methodology; Kalashnikova O contributed to software; Isupova E, Gaidar E, and Sorokina L contributed to validation; Raupov R contributed to formal analysis; Kaneva M, Masalova V, Dubko M, and Kornishina T contributed to investigation; Isupova E and Gaidar E contributed to resources; Kalashnikova O and Chikova I contributed to data curation; Kostik M, Lubimova NA, and Kuchinskaya E contributed to funding; Kaneva M contributed to visualization; Kostik M contributed to supervision, project administration; All authors have read and approve the final manuscript.

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Institutional review board statement: Written consent was obtained according to the declaration of Helsinki. The Ethics Committee of Saint Petersburg State Pediatric Medical University (protocol number 1/3 from 11.01.2021) approved this retrospective study's protocol.

Informed consent statement: All patients or patients' representatives (for patients under the age of 15) gave their consent in their case.

report forms authorizing the anonymous use of their medical information. All patients were appropriately anonymized.

Conflict-of-interest statement: All the authors declare that they have no conflict of interest.

Data sharing statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

STROBE statement: The authors have read the STROBE Statement – checklist of items, and the manuscript was prepared and revised according to the STROBE Statement – checklist of items.

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Country/Territory of origin: Russia

ORCID number: Elvira Kalashnikova 0000-0002-4932-0588; Eugenia Isupova 0000-0002-0911-7817; Ekaterina Gaidar 0000-0002-0971-2018; Lyubov Sorokina 0000-0002-9710-9277; Maria Kaneva 0000-0003-4325-0125; Vera Masalova 0000-0002-3703-4920; Margarita Dubko 0000-0002-6834-1413; Tatiana Kornishina 0000-0002-6238-4121; Natalia Lubimova 0000-0002-5782-8373; Ekaterina Kuchinskaya 0000-0002-1383-3373; Irina Chikova 0000-0003-4636-5825; Rinat Raupov 0000-0001-7749-6663; Olga Kalashnikova 0000-0002-8683-4270; Mikhail Kostik 0000-0002-1180-8086.

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REFERENCES

- Fava A, Petri M. Systemic lupus erythematosus: Diagnosis and clinical management. *J Autoimmun* 2019; **96**: 1-13 [PMID: 30448290 DOI: 10.1016/j.jaut.2018.11.001]
- Fanourakis A, Kostopoulou M, Alunno A, Aringer M, Bajema I, Boletis JN, Cervera R, Doria A, Gordon C, Govoni M, Houssiau F, Jayne D, Kouloumas M, Kuhn A, Larsen JL, Lerström K, Moroni G, Mosca M, Schneider M, Smolen JS, Svenungsson E, Tesar V, Tincani A, Trolldborg A, van Vollenhoven R, Wenzel J, Bertsias G, Boumpas DT. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis* 2019; **78**: 736-745 [PMID: 30926722 DOI: 10.1136/annrheumdis-2019-215089]
- Watson L, Beresford MW, Maynes C, Pilkington C, Marks SD, Glackin Y, Tullus K. The indications, efficacy and adverse events of rituximab in a large cohort of patients with juvenile-onset SLE. *Lupus* 2015; **24**: 10-17 [PMID: 25117653 DOI: 10.1177/0961203314547793]
- Thakral A, Klein-Gitelman MS. An Update on Treatment and Management of Pediatric Systemic Lupus Erythematosus. *Rheumatol Ther* 2016; **3**: 209-219 [PMID: 27747587 DOI: 10.1007/s40744-016-0044-0]
- Sawhney S, Agarwal M. Rituximab use in pediatric systemic lupus erythematosus: Indications, efficacy and safety in an Indian cohort. *Lupus* 2021; **30**: 1829-1836 [PMID: 34315295 DOI: 10.1177/09612033211034567]
- Abdirakhmanova A, Sazonov V, Mukusheva Z, Assylbekova M, Abdulkhakimova D, Poddighe D. Macrophage Activation Syndrome in Pediatric Systemic Lupus Erythematosus: A Systematic Review of the Diagnostic Aspects. *Front Med (Lausanne)* 2021; **8**: 681875 [PMID: 34150813 DOI: 10.3389/fmed.2021.681875]
- Gasparotto M, Gatto M, Binda V, Doria A, Moroni G. Lupus nephritis: clinical presentations and outcomes in the 21st century. *Rheumatology (Oxford)* 2020; **59**: v39-v51 [PMID: 33280015 DOI: 10.1093/rheumatology/keaa381]
- Parikh SV, Alamaani S, Brodsky S, Rovin BH. Update on Lupus Nephritis: Core Curriculum 2020. *Am J Kidney Dis* 2020; **76**: 265-281 [PMID: 32220510 DOI: 10.1053/j.ajkd.2019.10.017]
- Moroni G, Vercelloni PG, Quaglini S, Gatto M, Gianfreda D, Sacchi L, Raffiotta F, Zen M, Costantini G, Urban ML, Pieruzzi F, Messa P, Vaglio A, Sinico RA, Doria A. Changing patterns in clinical-histological presentation and renal outcome over the last five decades in a cohort of 499 patients with lupus nephritis. *Ann Rheum Dis* 2018; **77**: 1318-1325 [PMID: 29730634 DOI: 10.1136/annrheumdis-2017-212732]
- Basu B, Roy B, Babu BG. Efficacy and safety of rituximab in comparison with common induction therapies in pediatric active lupus nephritis. *Pediatr Nephrol* 2017; **32**: 1013-1021 [PMID: 28191596 DOI: 10.1007/s00467-017-3583-x]
- Ruiz-Irastorza G, Bertsias G. Treating systemic lupus erythematosus in the 21st century: new drugs and new perspectives on old drugs. *Rheumatology (Oxford)* 2020; **59**: v69-v81 [PMID: 33280011 DOI: 10.1093/rheumatology/keaa403]
- Li K, Yu Y, Gao Y, Zhao F, Liang Z, Gao J. Comparative Effectiveness of Rituximab and Common Induction Therapies for Lupus Nephritis: A Systematic Review and Network Meta-Analysis. *Front Immunol* 2022; **13**: 859380 [PMID: 35444666 DOI: 10.3389/fimmu.2022.859380]
- Looney RJ, Anolik JH, Campbell D, Felgar RE, Young F, Arend LJ, Sloand JA, Rosenblatt J, Sanz I. B cell depletion as a novel treatment for systemic lupus erythematosus: a phase I/II dose-escalation trial of rituximab. *Arthritis Rheum* 2004; **50**: 2580-2589 [PMID: 15334472 DOI: 10.1002/art.20430]
- Looney RJ, Anolik J, Sanz I. B cells as therapeutic targets for rheumatic diseases. *Curr Opin Rheumatol* 2004; **16**: 180-185 [PMID: 15103242 DOI: 10.1097/00002281-200405000-00003]
- Leandro MJ, Edwards JC, Cambridge G, Ehrenstein MR, Isenberg DA. An open study of B lymphocyte depletion in systemic lupus erythematosus. *Arthritis Rheum* 2002; **46**: 2673-2677 [PMID: 12384926 DOI: 10.1002/art.10541]
- Ramos-Casals M, Soto MJ, Cuadrado MJ, Khamashta MA. Rituximab in systemic lupus erythematosus: A systematic review of off-label use in 188 cases. *Lupus* 2009; **18**: 767-776 [PMID: 19578100 DOI: 10.1177/0961203309106174]

- 17 **Stolyar L**, Lahita RG, Panush RS. Rituximab use as induction therapy for lupus nephritis: a systematic review. *Lupus* 2020; **29**: 892-912 [PMID: 32486934 DOI: 10.1177/0961203320928412]
- 18 **Fanourakis A**, Tziolos N, Bertsias G, Boumpas DT. Update on the diagnosis and management of systemic lupus erythematosus. *Ann Rheum Dis* 2021; **80**: 14-25 [PMID: 33051219 DOI: 10.1136/annrheumdis-2020-218272]
- 19 **Athanassiou P**, Athanassiou L. Current Treatment Approach, Emerging Therapies and New Horizons in Systemic Lupus Erythematosus. *Life (Basel)* 2023; **13** [PMID: 37511872 DOI: 10.3390/life13071496]
- 20 **Petri M**. SLICC classification criteria for systemic lupus erythematosus. Available from: <https://sliccgroup.org/research/sle-criteria/>
- 21 **Mosca M**, Bombardieri S. Assessing remission in systemic lupus erythematosus. *Clin Exp Rheumatol* 2006; **24**: S-99 [PMID: 17083771]
- 22 **Parodi A**, Davi S, Pringe AB, Pistorio A, Ruperto N, Magni-Manzoni S, Miettunen P, Bader-Meunier B, Espada G, Sterba G, Ozen S, Wright D, Magalhães CS, Khubchandani R, Michels H, Woo P, Iglesias A, Guseinova D, Bracaglia C, Hayward K, Wouters C, Grom A, Vivarelli M, Fischer A, Breda L, Martini A, Ravelli A; Lupus Working Group of the Paediatric Rheumatology European Society. Macrophage activation syndrome in juvenile systemic lupus erythematosus: a multinational multicenter study of thirty-eight patients. *Arthritis Rheum* 2009; **60**: 3388-3399 [PMID: 19877067 DOI: 10.1002/art.24883]
- 23 **Gul H**, Mushtaq MS, Salim B, Samreen S, Nasim A, Khan M. A Comparison Of Mycophenolate Mofetil And Cyclophosphamide As Lupus Nephritis Induction Therapy. *J Ayub Med Coll Abbottabad* 2020; **32**: 454-458 [PMID: 33225643]
- 24 **Rovin BH**, Furie R, Latinis K, Looney RJ, Fervenza FC, Sanchez-Guerrero J, Maciua R, Zhang D, Garg JP, Brunetta P, Appel G; LUNAR Investigator Group. Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study. *Arthritis Rheum* 2012; **64**: 1215-1226 [PMID: 22231479 DOI: 10.1002/art.34359]
- 25 **Zhang J**, Zhao Z, Hu X. Effect of Rituximab on Serum Levels of Anti-C1q and Antineutrophil Cytoplasmic Autoantibodies in Refractory Severe Lupus Nephritis. *Cell Biochem Biophys* 2015; **72**: 197-201 [PMID: 25490907 DOI: 10.1007/s12013-014-0437-z]
- 26 **Tambralli A**, Beukelman T, Cron RQ, Stoll ML. Safety and efficacy of rituximab in childhood-onset systemic lupus erythematosus and other rheumatic diseases. *J Rheumatol* 2015; **42**: 541-546 [PMID: 25593242 DOI: 10.3899/jrheum.140863]
- 27 **Kalashnikova EM**, Raupov RK, Lyubimova NA, Kuchinskaya EM, Masalova VV, Isupova EA, Gaidar EV, Dubko MF, Snegireva LS, Sorokina LS, Kornishina TL, Kaneva MA, Chikova IA, Likhacheva TS, Kolobova OL, Kalashnikova OV, Chasnyk VG, Kostik MM. The experience of rituximab therapy in patients with juvenile systemic lupus erythematosus: the preliminary results of two-center cohort study. *Rossiyskiy Vestnik Perinatologii i Pediatrii* 2023; **68**: 74-84 [DOI: 10.21508/1027-4065-2023-68-1-74-84]
- 28 **Kostik M**, Kalashnikova E, Rinat R, Isupova E, Gaidar E, Soloviev AA, Masalova V, Snegireva L, Kornishina T, Abramova N, Suspitsin E, Sorokina L, Kaneva M, Dubko MF, Lyubimova N, Kuchinskaya E, Kalashnikova O, Chasnyk V. Rituximab Biosimilar BCD020 Shows Superior Efficacy above Conventional Non-Biologics Treatment in Pediatric Lupus Nephritis: The Data of Retrospective Cohort Study. *Biomedicines* 2023; **11** [PMID: 37239173 DOI: 10.3390/biomedicines11051503]
- 29 **Zhong Z**, Li H, Zhong H, Zhou T. Clinical efficacy and safety of rituximab in lupus nephritis. *Drug Des Devel Ther* 2019; **13**: 845-856 [PMID: 30880917 DOI: 10.2147/DDDT.S195113]
- 30 **Chan EY**, Wong SW, Lai FF, Ho TW, Tong PC, Lai WM, Ma AL, Yap DY. Long-term outcomes with rituximab as add-on therapy in severe childhood-onset lupus nephritis. *Pediatr Nephrol* 2023; **38**: 4001-4011 [PMID: 37358717 DOI: 10.1007/s00467-023-06025-6]
- 31 **Bag-Ozbek A**, Hui-Yuen JS. Emerging B-Cell Therapies in Systemic Lupus Erythematosus. *Ther Clin Risk Manag* 2021; **17**: 39-54 [PMID: 33488082 DOI: 10.2147/TCRM.S252592]
- 32 **Hui-Yuen JS**, Nguyen SC, Askanase AD. Targeted B cell therapies in the treatment of adult and pediatric systemic lupus erythematosus. *Lupus* 2016; **25**: 1086-1096 [PMID: 27497253 DOI: 10.1177/0961203316652491]
- 33 **Mahmoud I**, Jellouli M, Boukhris I, Charfi R, Ben Tekaya A, Saidane O, Ferjani M, Hammi Y, Trabelsi S, Khalfallah N, Tekaya R, Gargah T, Abdelmoula L. Efficacy and Safety of Rituximab in the Management of Pediatric Systemic Lupus Erythematosus: A Systematic Review. *J Pediatr* 2017; **187**: 213-219.e2 [PMID: 28602379 DOI: 10.1016/j.jpeds.2017.05.002]



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