

Systemic Lupus Erythematosus: relationship between different treatments and clinical evolution

Lúpus Eritematoso Sistêmico: relação entre os diferentes tratamentos e evolução clínica

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Macedo RM, Garcia TR, Castanheira EP, Noleto DC, Freitas TVM, Freitas AA. Systemic lupus erythematosus: relationship between different treatments and clinical evolution / *Lúpus eritematoso sistêmico: relação entre os diferentes tratamentos e evolução clínica*. Rev Med (São Paulo). 2020 Nov-Dec;99(6):573-80.

ABSTRACT: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease of autoimmune origin that presents variable clinical manifestations, being progressive and potentially fatal, if not treated. Standard treatments include antimalarials, corticosteroids (CS) and immunosuppressants. However, despite a better understanding of the disease process, there is still a significant and unmet need for new treatment due to the continued high risk of mortality and progression of organ damage. Thus, the objective of the present study was making a bibliographical survey about the different treatments published for the management of SLE related to the patient's clinical improvement. For that, the Lilacs, Scielo, PubMed and Google Scholar databases were used, and the Health Sciences Descriptors (DeCS) used were: "systemic lupus erythematosus", "therapeutics" and "quality of life". The selected articles were published in English and Portuguese, between the years 2014 and 2020. The references found showed that antimalarials and the infusion of fresh frozen plasma are the most effective therapeutic resources. In addition, vitamin D supplementation showed to have a beneficial function under the clinical picture of lupus patients. Another effective treatment for skin lesions was the use of pulsed dye laser. Thus, further studies are needed on demonstrating the effectiveness of different treatments for SLE in order to elucidate the efficacy and safety of the different therapies used.

Keywords: Lupus erythematosus, systemic; Immunosuppressive agents; Quality of life; Therapeutics.

RESUMO: O Lúpus Eritematoso Sistêmico (LES) é uma doença inflamatória crônica de origem autoimune que apresenta manifestações clínicas variáveis, sendo progressiva e potencialmente fatal, se não tratado. Os tratamentos padrões incluem antimaláricos, corticosteroides (CS) e imunossupressores. No entanto, apesar do melhor entendimento do processo da doença, ainda há uma necessidade significativa e não atendida de novo tratamento devido ao alto risco continuado de mortalidade e progressão de danos aos órgãos. Assim, o objetivo do presente estudo foi fazer um levantamento bibliográfico acerca dos diferentes tratamentos publicados para o manejo do LES relacionando com a melhora clínica do paciente. Para tanto, utilizou-se as bases de dados Lilacs, SciELO, PubMed e Google Acadêmico e os Descritores em Ciências da Saúde (DeCS) utilizados foram: "lúpus eritematoso sistêmico", "terapêutica" e "qualidade de vida". Os artigos selecionados foram publicados em língua inglesa e portuguesa, entre os anos de 2014 e 2020. As referências encontradas permitiram constatar que os antimaláricos e a infusão de plasma fresco congelado são os recursos terapêuticos com maior eficácia. Além disso, a suplementação com vitamina D apresentou mostrou ter função benéfica sob o quadro clínico de pacientes lúpicos. Outro tratamento efetivo para as lesões dermatológicas foi a utilização de laser de corante pulsado. Desse modo, são necessários mais estudos acerca da demonstração da eficácia dos diferentes tratamentos para o LES, a fim de elucidar a eficácia e a segurança das diversas terapias utilizadas.

Palavras-chave: Lúpus eritematoso sistêmico; Imunossupressores; Qualidade de vida; Terapêutica.

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INTRODUCTION

The Systemic Lupus Erythematosus (SLE) corresponds to a chronic and inflammatory autoimmune disease characterized, mainly, by the loss of tolerance to nucleic acids and their binding proteins, which its pathophysiology can be explained by the generation of antinuclear antibodies (ANAs), formation and deposition of immunocomplexes in various organs and tissues. Its etiology is still unknown, and may be related to environmental, hormonal, immunological or genetic factors. Presents variable clinical manifestations, and it can be progressive and potentially fatal, if not treated^{1,2,3}.

Worldwide, the incidence rates of SLE ranged from around 0,3 to 23,7 out of 100.000 people/year, meanwhile the prevalence of cases was from 6,5 to 178,0 out of 100.000, and the variations observed in this rates reflect differences of age, gender, ethnical origin, socioeconomic condition and geographic region of the patients. Presents a higher prevalence in adults, women of childbearing age and non-Caucasians, as afro descendants, for example. In Brazil, it is estimated an SLE incidence of around 8,7 cases out of 100.000 people/year, and mortality is about 3 to 5 times higher than that of the general population^{4,5}.

As a multisystemic disease, it presents a heterogeneity of clinical manifestations with periods of accentuation and remission. The clinical picture includes the presence of monocutaneous manifestations, among which malar erythema and photosensitivity, in addition to oral ulcers, renal, cardiac, neurological, musculoskeletal and hematological impairment. Often, immunological manifestations such as the presence of antinuclear antibodies (ANA) in the blood are also observed^{5,6}.

Regarding the diagnosis of SLE, the most accepted and well-disseminated criterion is that proposed by the American College of Rheumatology (ACR) in 1982, which establishes that the presence of SLE can be confirmed by pricing at least 4 of the following 11 classification criteria: malar erythema, discoid injury, photosensitivity, oral ulcer, arthritis, serositis (pleurite or pericarditis), renal alteration (proteinuria or cell cylinders), neurological disorders (convulsion or psychosis), hematological changes (hemolytic anemia with reticulocytosis, leukopenia, lymphopenia or thrombocytopenia), immunological changes (presence of native anti-DNA, anti-Sm or antiphospholipid antibodies) and antinuclear factors (ANF).

The development of therapies for SLE was limited by clinical and biological heterogeneity, including the diversity of gene expression signatures in peripheral blood patients. Standard treatments include antimalarials, corticosteroids (CS) and immunosuppressants. However, despite a better understanding of the disease process, there is still a significant and unmet need for new treatment due to continued high risk of mortality and progression of organ damage. In addition, chronic burden of symptoms

and toxicity of immunosuppressive therapies also have a significant impact on the patient's quality of life.

Several medications operate by modulating the immune system of the patients, since a fundamental aspect of SLE is the participation of B lymphocytes in the pathogenicity of the disease, once these cells are activated and from there migrate to different regions, where they undergo clonal expansion, proliferating, and forming the lymphoid aggregates that are deposited in the tissues. Among the most frequently used medications, there is Hydroxychloroquine, which acts by inhibiting the B-cell receptor and signaling; Cyclophosphamide, an annihilating agent of B and T cells and suppressor of antibody production; rituximab, anti-CD20 monoclonal antibody that leads to peripheral B-cell depletion; belimumab, responsible for reducing circulating B cells; calcineurin inhibitors such as cyclosporine and immunosuppressants such as Azathioprine, mycophenolate and tacrolimus.

In view of the above, it is evident that SLE is a disease that negatively affects the quality of life of the affected individuals, bringing unfavorable symptoms to their survival, besides not presenting definitive cure. Thus, the aim of this study was to make a bibliographic survey about the different treatments published for the management of SLE related to the clinical improvement of the patient.

MATERIAL AND METHODS

This study refers to a bibliographic review with a qualitative approach, with a descriptive objective of national and international studies. The following steps were used to construct this review: identification of the theme; selection of the research question; data collection by searching the literature, in electronic databases, with establishment of inclusion criteria to select the sample; elaboration of an data collection instrument with the information to be extracted; evaluation of the studies included in the integrative review; interpretations of the results and presentation of the evidenced results.

For the preparation of the study, a search was carried out for productions in the databases *Literatura Latino Americana e do Caribe em Ciências da Saúde (Lilacs)*, Scientific Electronic Library Online (SciELO), Public Medlines (PubMed) and Academic Google. For the choice of the appropriate descriptors for the body of work and corresponding to the study, a search was performed on the basis of *Descritores em Ciências da Saúde (DeCS)*, resulting in the following descriptors: "systemic lupus erythema", "therapeutic" and "quality of life". Besides this selection, to select the studies that best contributed to the research, Boolean operators were used, which were: "parentheses", "AND" and "OR".

With this, the articles that were fully available were filtered, in sequential order, indexed with a contained

time frame in the last 5 years and in the following idioms: English and Portuguese. The including criteria of inclusion were: articles that elucidate patients, regarding their ethnic or gender; studies that presented physiopathology and brought data referring to both treatments (SLE and their level of efficacy); and approached the quality of life of the patients in relation to the type of treatment adopted.

Besides, the articles that were not available in full, were duplicated and opinion articles were excluded.

RESULTS AND DISCUSSION

The Chart 1 contains the main treatments found in modern literature to the treatment of SLE.

Chart 1: characterization of the main analyzed studies

Writers/Year	Journal - <i>Qualis</i>	Objective	Main founds
Aranow et al. 2015	Arthritis Rheumatol. <i>Qualis</i> A1	Investigate the effects of vitamin D supplementation on the IFN sign in patients with SLE.	Vitamin D supplementation up to 4000 IU daily was safe and well tolerated but did not decrease IFN signature in patients with SLE with vitamin D deficiency ¹⁹ .
Witcher et al. 2015	Brit J Clin Pharmacol. <i>Qualis</i> A1	Evaluate the pharmacokinetics safety and biological activity of tabalumab, administered intravenously or subcutaneously in individuals with rheumatoid arthritis or SLE.	A single dose of tabalumab administered was well tolerated. Tabalumab showed biological activity based on changes in peripheral numbers of CD20+ lymphocytes in both individuals with AR and SLE ²⁵ .
Mejía-Vilet et al. 2016	Clin Rheumatol. <i>Qualis</i> A4	Evaluate the response to immunosuppressive treatment of Hispanics with pure membranous lupus nephritis (MLN).	Mycophenolate mofetil MMF may be superior to intravenous Cyclophosphamide, while Azathioprine may remain a valid alternative to the treatment ²⁶ .
Rovin et al. 2016	SAGE J. <i>Qualis</i> B4	Evaluate the safety and efficacy of tabalumab on the SLE treatment.	Tabalumab resulted in a significant reduction in B cells and decreased levels of immunoglobulin G at both doses. There were no significative signs of kidney safety ¹⁴ .
Lima et al. 2017	Osteoporosis Int. <i>Qualis</i> A2	Evaluate the effect of vitamin D supplementation in patients with juvenile-onset systemic lupus erythematosus (JoSLE).	Cholecalciferol supplementation for 24 weeks effectively improved bone microarchitecture parameters in patients with vitamin D supplementation ²⁷ .
Ekinci; Ozturk 2017	SAGE J. <i>Qualis</i> B4	The aim of this report was to share experience on the course of management of three cases diagnosed as SLE with C1q deficiency, in the light of the current literature.	This report suggests that severe skin lesions as observed in these patients with SLE with C1q deficiency, cannot be controlled with conventional immunosuppressive treatment. Instead, regular infusions of fresh plasma are proposed as a more reasonable treatment method ¹⁶ .
Furlan et al. 2018	Rev Soc Bras Clín Med. <i>Qualis</i> C	Evaluate whether the overall well-with SLE is affected by the use of antimalarials.	The use of antimalarials was associated with a lower occurrence of psychosis and kidney lesions, although it has led to a higher frequency of seizures. Regarding individual perception of quality of life, there was no significant difference between the three groups ¹² .
Vollenhoven et al. 2018	Lancet <i>Qualis</i> A1	Evaluate the efficacy and safety of Ustecinumab in the treatment of SLE in patients with moderate to severe activity despite conventional treatment.	The addition of Ustecinumab to standard treatment resulted in better efficacy in clinical and laboratory parameters than placebo in the treatment of active SLE. The results support the development of Ustecinumab as a new treatment for systemic lupus erythematosus ¹¹ .
Lai et al. 2018	Lancet <i>Qualis</i> A1	Evaluate the safety, tolerance and efficacy of Sirolimus in an open-up, prospective, biomarker-controlled clinical study.	The data show that a progressive improvement of the disease activity is associated with the correction of the specification of the pro-inflammatory T-cell lineage in patients with active systemic lupus erythematosus during 12 months of treatment with Sirolimus ²¹ .

Chart 1: Characterization of the main analyzed studies

continuation

Writers/Year	Journal - <i>Qualis</i>	Objective	Main founds
Kraaij et al. 2018	J Autoimmunity <i>Qualis A1</i>	Investigate whether the interference in the formation of immunocomplexes using a combination of rituximab (RTX) and belimumab (BLM), can decrease the formation of NETs and improve the disease.	The RTX þ BLM appeared to be safe and obtained clinically significant responses: low lupus disease status was achieved in 10 patients, kidney responses in 11 patients and concomitant immunosuppressive medication was reduced in 14 out of the 16 patients ³ .
Mendez et al. 2018	Am Soc Nephrol. <i>Qualis A1</i>	Characterize the variability of B-cell depletion in peripheral blood after rituximab and evaluate its association with complete response in patients with lupus nephritis.	There was substantial variability in B-cell depletion in peripheral blood in patients with lupus nephritis treated with rituximab in the study ⁹ .
Zhang et al. 2018	Clin Rheumatol. <i>Qualis B2</i>	Evaluate the efficacy and safety of a 24-week course with low-dose Leflunomide combined with prednisone in the induction treatment of proliferative lupus nephritis in Chinese patients.	Compared to Cyclophosphamide, low dose Leflunomide in combination with prednisone showed efficacy and safety in induction therapy of proliferative lupus nephritis in Chinese patients ²² .
An et al. 2018	Int League Assoc Rheumatol. <i>Qualis B2</i>	Seek higher remission rate of lupus nephritis using a combined strategy.	Treatment with a combined immunosuppressive agent is superior to routine Cyclophosphamide-only therapy in lupus nephritis ²³ .
Ishii et al. 2018	Japan Col Rheumatol. <i>Qualis A2</i>	Evaluate the efficacy and safety of bortezomib in the treatment of SLE in patients whose disease activity could not be controlled.	As bortezomib therapy for SLE is associated with many adverse reactions, the treatment indications with many adverse reactions should be carefully selected, and the protocols should aim to prevent such occurrences ¹⁵ .
Wallace et al. 2018	Lancet <i>Qualis A1</i>	Evaluate the efficacy, safety and tolerability of oral Baricitinib in patients with active SLE, that were receiving standard therapeutic treatment.	It was found that the daily use of 4 mg of Baricitinib showed improvement in SLE signs and symptoms, in addition to improving the clinical picture of patients with arthritis and joint pain. In other cases, it was observed that Baricitinib has positive effects under various dermatological conditions, such as atopic dermatitis, psoriasis and alopecia ¹³ .
Merrill et al. 2018	Arthritis Rheumatol. <i>Qualis A1</i>	Evaluate the efficacy and safety of Atacicept, a B-lymphocyte stimulator antagonist, in patients with SLE.	The treatment with Atacicept showed effective evidence in the treatment of SLE, particularly in APH and serologically active patients. Severe crises were observed, with acceptable safety profile ⁷ .
Gualtierotti et al. 2018	Clin Exp Rheumatol. <i>Qualis A3</i>	Description of three patients with active SLE who achieved disease control after sequential treatment with rituximab and belimumab and discussion of the logic behind it.	A beneficial effect was observed after sequential treatment with rituximab and belimumab. All the patients achieved long-standing remission and were able to reduce or discontinue corticosteroids ²⁸ .
Conceição et al. 2019	Adv. Rheumatol. <i>Qualis C</i>	Evaluate the effectiveness of psychoanalytic psychotherapy in a brief group to improve quality of life, depression, anxiety and coping strategies in patients with SLE.	Psychoanalytic psychotherapy was effective in improving many aspects of quality of life and a positive coping ability, in addition to reducing SLE symptoms, anxiety and depression levels ²⁴ .
Ototake et al. 2019	Jpn. Dermatol. <i>Qualis A1</i>	Investigate the efficacy of Hydroxychloroquine in the treatment of skin manifestations according to LEC subtypes in Japanese patients.	Overall, HCQ was highly effective for the skin, as 87% of patients had at least some beneficial response in at least one type of skin lesion. In 74% of patients treated with concomitant systemic therapy, all disease activity decreased by about 32 weeks by additional administration of HCQ ¹⁷ .

Source: articles used to the realization of the study.

Extracellular neutrophil traps (NETs) have been demonstrated as prominent autoantigens, leading to the production of autoantibodies relevant to the disease. In addition to NETs, which are proposed as important autoantigens for the development of ANAs, patients with SLE have hyperactivity characteristics of B lymphocytes, including the typical increase in circulating plasmocytes. Experimentally, it was observed that if these cells were removed from mouse “lupus models” by genetic manipulation or antibody therapy, the chain of immune reactions would be largely suppressed, including T-cells induced abnormalities^{2,3}.

The combined use of rituximab and belimumab (RTX þ BLM) caused preferential reductions in autoantibody levels compared to physiological levels of antibodies, suggesting that autoantibody-secreting plasmocytes are more susceptible to this treatment. It has also been shown that RTX þ BLM has improved autoimmune phenomena by reducing circulated ANAs and regressing excessive formation of NETs mediated by immunocomplexes in SLE. Simultaneously, the RTX þ BLM caused significant clinical responses in patients with severe refractory SLE. The therapy with RTX þ BLM represents a promising new concept of treatment aimed specifically at autoimmunity in patients with SLE³.

Another study compared the efficacy and safety of two doses of atacept (75 and 150 mg) with placebo in patients with active SLE and with antibody level based on the fact that elevated serum levels of BLyS (B lymphocyte stimulator) and APRIL (a proliferation inducer) in patients with SLE correlate with disease activity and production of autoantibodies. These factors were promising goals for new research therapies and from this, the efficacy of atacept, the double inhibitor APRIL and BLyS, was also suggested by this study, confirming its biological activity in the total reduction of B cells, plasmocytes and immunoglobulin in patients with SLE⁷.

Another recently investigated therapy for the treatment of SLE is Ustecinumab, which is a drug based on a monoclonal antibody, which binds to the p40 subunit by interleukin 12 and interleukin 23, the main inflammatory cytokines of the body. Its use has been shown to be effective in the treatment of SLE since it has as its main benefit the reduction of outbreaks of the disease after the 12th week of use. There has also been a considerable reduction in the number of autoantibodies and complement protein C3 in the bloodstream. It was considered effective for a both local and systemic treatment. The main disadvantage found was the increase in the number of urinary tract and nasopharynx infections, headache and respiratory diseases in the case group¹¹.

In addition to investigations into alternative therapies to SLE, another medicine used in the treatment is antimalarials, which are associated with a lower occurrence of psychosis and lesions, although it led to

a higher frequency of seizures in lupus patients. The individual perception of quality of life showed that the use of antimalarials (ATM) has no influence on the well-being of patients, except for mental health in tobacco users. The evidences allow us to consider ATM as safe drugs, which have more clinical benefits than adverse effects¹².

Another point worth mentioning is that, despite the numerous advances in treatment for SLE, this disease remains with a high rate of morbidity and mortality. Recent studies show that Baricitinib, especially when used 4 mg/day, is associated with significant clinical improvements in lupus patients. However, further studies on Baricitinib as a potential therapy for patients with SLE are needed¹³.

From the disease pathophysiology, it is important to highlight that in patients with SLE, B-cell activation factor (BAFF) levels are high. Thus, tabalumab, which is a monoclonal antibody that neutralizes the membrane, and soluble BAFF has been shown to be effective in reducing disease activity. This medicinal product had significant pharmacodynamic effects on the number of B cells and IgG levels. However, after one year of treatment in patients with moderate to severe active SLE, but without severe active lupus nephritis, tabalumab had no effects compared to placebo in the ITT population (patients intending to treat)¹⁴.

Although many strategies targeting B-cell lines have been recently investigated, only belimumab has been approved for SLE therapy by *Food and Drug Administration* (FDA) from the USA. The bortezomib is a proteasome inhibitor that has been approved for the treatment of multiple myeloma (MM). However, the proteasome inhibitor also works effectively as an inhibitor to produce pro-inflammatory cytokines by regulating NF-κB activation. A recent study investigated the effects of bortezomib in patients with persistent SLE, despite the use of immunosuppressive therapies. In this small uncontrolled study, disease activity decreased significantly with treatment with bortezomib. These studies suggest that bortezomib can be effective in treating various symptoms of SLE by means of a mechanism other than inhibition of the production of anti-dsDNA antibodies. Therefore, for the indication of this treatment it is necessary to analyze each case individually and verify if the treated symptom really is of great importance for the treatment and improvement of the quality of life of the patient¹⁵.

It is known that hereditary deficiency of the early components of the complement system, especially C1q deficiency, is one of the reasons for early-onset SLE. Evidences suggest that the regular infusion of fresh frozen plasma (FFP) for the treatment of patients with SLE associated with C1q deficiency is of high efficacy, despite the risks of infection, hypocalcemia and acute lung injury associated with this type of transfusion are considerably low. It is observed that FFP administration normalizes the level of C1q for a very short period of time, however considerable and significant for the improvement of the

patient's clinical picture¹⁶.

Another factor to be considered is that there is evidence to support the involvement of the interferon pathway type I in SLE. In this sense, the therapeutic benefit of the interferon pathway inhibition in patients with SLE has been reported in a study of the use of anifrolumab, a fully human IgG1 κ monoclonal antibody for type I interferon receptor subunit 1 inhibiting signaling by all type I interferons. Patients receiving anifrolumab were more likely to reduce glucocorticoid dose and severity of skin disease than patients receiving placebo. However, the differences between the groups in relation to swollen and sore joint counts and the updated rate of SLE seizures were not significant. Furthermore, this study was not designed to determine the durability of the effect or risks beyond 52 weeks⁸.

A retrospective analysis of the efficacy of Hydroxychloroquine (HCQ) in skin treatment suggests that HCQ is shown to be extremely effective in the minimization of skin lesions. On the other hand, it was found that patients with SLE who had these skin lesions were more sensitive to treatment with HCQ, as they had adverse effects to the detriment of improved signs and symptoms. There are several limitations in this research, since it was a small retrospective study and enrolled patients with different backgrounds, with different severities and durations of the disease. These factors can significantly affect the efficacy of HCQ, but further studies, with longer duration and with more significant samples, are needed to better verify the efficacy of this medicinal product in question¹⁷.

The randomized, double-blind study showed that vitamin D supplementation (cholecalciferol 50,000 IU/week for six months) in patients with juvenile lupus improved bone microarchitecture, with the tibia as parameter. Another advantage of this study was that the treatment of patients with vitamin D supplementation remained stable during the six months of follow-up, thus allowing a more accurate analysis of the effect of this supplementation on this rheumatic condition¹⁸.

Another study suggests that vitamin D modulates immune response and blocks the induction of interferon (IFN) serum from patients with SLE. This research analyzed the potential impact of vitamin D3 supplementation in the overexpression of IFN-inducible genes in patients with SLE with vitamin D deficiency, and it was not observed reduction in IFN signature response after 12 weeks of vitamin D supplementation compared to placebo¹⁹.

A randomized research into the efficacy and safety of pulsed dye laser (PDL) in the treatment of lupus skin lesions suggests that lesions treated with PDL showed a significant higher decrease in erythema index and texture index compared to the control. Curiously, the polymerase chain reaction in real time showed a reduction in cytokines CXCL-9, 10, IFN- γ , IL-1 β , TNF- α and TGF- β . In addition, the post-treatment lupus lesions showed a decrease in CD3,

CD4, CD8 and CXCR3 positive cells²⁰.

In a clinical and prospective study, rapamycin has been found to inhibit the proliferation of T lymphocytes and has been developed as a medicine under the generic designation of Sirolimus. In this research, the use of Sirolimus for SLE treatment has been satisfactory, as it showed a progressive improvement in disease activity. Which would be associated with the pro-inflammatory T-cell lineage in these patients. However, it is clear that further placebo-controlled clinical studies using Sirolimus are necessary, as a therapy in the various populations, in order to better elucidate the mechanism of action and efficacy of this drug in improving the quality of life of lupus patients²¹.

One of the new treatments with the best test result in the testing phase was Ustecinumab. The drug based on all-human monoclonal antibodies directed to the p40 subunit shared by interleukin 12 and 23 has just passed from phase 2 to phase 3, now being applied on a much larger scale. It was demonstrated sharp reduction in disease outbreaks, improvement in autoantibody and C3 protein levels and the possibility of both local and systemic treatment¹¹.

The treatment of membranous lupus nephritis (MLN) obtained promising results with the use of mycophenolate mofetil (MMF) and Azathioprine (AZA). The use of both drugs led to a complete remission rate of 76.4% and 54.6% of each disease respectively and more than 89% responded to treatment of AZA and MMF alone. The study analyzed its combined use of corticosteroids in the Hispanic population and, with the results obtained, it is intended to continue the study with different ethnicities to ensure that the genetic factor of the population analyzed is not a determinant in the expected response to medicinal products¹².

Cyclophosphamide was a medicine tested as an alternative to Leflunomide in the treatment of proliferative lupus nephritis. Its use in conjunction with glucocorticoids has had results close to standard treatments. Reduction of anti-dsDNA autoantibodies and proteinuria decreased significantly after ingestion of the combined medicinal product. However, the treatment is still limited, like the other ones, due to the fact that the small public analyzed (Chinese population) and the gene specificity that ethnicity can bring to treatment, with difficulty in generalizing its benefits and harms to other people²².

Another recent study, made in 2018, demonstrated the combined use of medicinal products through combined immunosuppressive treatment (CIST). The application of Cyclophosphamide, Hydroxychloroquine and some immunosuppressive agent has been shown to be superior to exclusive Cyclophosphamide therapy in the induction of remission in patients with lupus nephritis. The remission rate increased considerably from 20.8% of alone treatment to 39.5% and a lower treatment failure rate. However, the recurrence rate of the disease was constant in both

medications, with an average of 6 months of the return of the initial symptoms²³.

In addition to conventional medical treatment, research reveals the importance of the psychological role in the treatment of SLE. Psychological assistance prepares patients for the symptoms that are manifested and the social weight that the disease will bring, serving as a complementation to the usual pharmacological treatment. The author also highlights a lower frequency of symptoms, lower level of anxiety and depression, and increased access to medical treatment. As much as the study has been shown to be beneficial, more research time is needed to understand how much the psychological factor can change the immune responses²⁴.

CONCLUSION

In the present study, the main treatments used

for SLE were presented. It was found that among the most effective are antimalarials medicine, such as Hydroxychloroquine, and infusion with fresh frozen plasma. In addition, vitamin D supplementation in these patients has a beneficial function under the clinical picture of lupus patients. An effective treatment for skin lesions also demonstrated in this study was with the use of pulsed dye laser.

However, many studies have not yet found, with complete safety, the benefits of these drugs in improving the quality of life of these patients, in addition, many of them showed relevant limitations especially regarding sample size and type of study. Therefore, further studies are needed on demonstrating the efficacy of the different treatments for SLE, with long-term follow-ups and the most satisfactory number of samples, to better elucidate the efficacy and safety of the various therapies used to improve the clinical picture of lupus patients.

Authors' Participation: *Rafaela Melo Macedo*: Reading and synthesis of the selected articles; Writing of the results and discussion; Formatting the text for submission to the Journal; Translation of the abstract into English. *Thais Ribeiro Garcia*: Reading and synthesis of the selected articles; Writing of the results and discussion; Collaboration with the writing of the abstract. *Eduarda Pereira Castanheira*: Abstract writing; Organization and citation of references. *Deborah Costa Noletto*: Writing of the introduction; Writing of the objectives; Translation of the abstract into English; Collaboration with the writing of the references. *Thales Vieira Medeiros Freitas*: Reading and synthesis of the selected articles; Writing of the results and discussion; Collaboration with the writing of the references. *Aline de Araújo Freitas*: Teaching Advisor of the text.

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Received: 2020, August 12

Accepted: 2020, November 17