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Background: Therapeutic apheresis (TA) represents a therapeutic option in pre-existing conditions or rheumatic diseases that occur during gestation. Although pregnancy is not a contraindication itself, due to the lack of evidence-based guidelines and the alleged risk of maternal and/or fetal adverse events, there is general resistance to its application during pregnancy.

Objectives: In this observational study we aimed to evaluate the efficacy and safety of TA in high-risk pregnancies in patients with rheumatic diseases, followed over a decade in a tertiary Center.

Methods: Between January 2005 and April 2019, 843 TA procedures were performed during 51 pregnancies in 43 patients: 745 plasma exchange sessions and 98 immunoadsorption sessions. TA was performed in 29 (57%) pregnancies of 21 (48.8%) patients with antiphospholipid antibody syndrome (APS), in 20 (39.2%) pregnancies of 20 (46.5%) patients with congenital heart block (CHB), in 1 (1.9%) pregnancy of 1 (2.3%) patient with systemic sclerosis (SSc) and 1 (1.9%) pregnancy of 1 (2.3%) patient affected by lupus nephritis (SLE).

Results: During the period considered, apheresis sessions applied to pregnant women were 7.1% of the total ($n = 13,251$). The average age at the first treatment was 33 years (range 24-43). The mean management age at the first apheretic treatment was 21 weeks (range 4-32). Twelve (1.4%) apheresis sessions were complicated by adverse events, none required or prolonged hospitalization. There were 44 (86.3%) live births, 3 (5.9%) spontaneous abortions and 2 (3.9%) voluntary terminations of pregnancy, 2 (3.9%) lost to follow-up. The average gestational age at birth was 35 weeks (range 24-37) and cesarean section was performed in 41 (80.4%) cases. TA was added to conventional therapy in 24/29 (82.7%) patients with APS, to the detection of fetal cardiac activity, while in 5/26 (17.3%) it was introduced when the first signs of pregnancy complications such as mild preeclampsia, HELLP and IUGR were detected. TA was started within 24 hours of atrioventricular block (AVB) detection; 10/20 (50%) mothers with CHB were diagnosed with 2nd degree AVB, 9/20 (45%) with 3rd degree AVB and one (5%) with sinus bradycardia and endocardial fibroelastosis. The patient with SSc was treated with TA twice a week from the 32nd SG until delivery, which occurred at the 36th SG, due to severe IUGR and oligohydramnios. The patient with SLE complicated by lupus nephritis was treated with TA twice a week, from the 26th SG until the birth, which took place at the 31st SG.

Conclusion: Our data have shown that TA in pregnancy is well tolerated. Close collaboration between rheumatologist, obstetrician and specialist in TA is essential to ensure a successful outcome of high-risk pregnancies.

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SAT0177

MULTITARGET THERAPY WITH TACROLIMUS AND MYCOPHENOLATE MOFETIL FOR TREATMENT OF LUPUS NEPHRITIS PRESENTED WITH RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

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Background: Although, most lupus nephritis patients present with chronic glomerulonephritis or nephrotic syndrome, some patients develop rapidly progressive glomerulonephritis (RPGN), which is a clinical syndrome characterized by rapid loss of renal function over a short period of time (days to months). Multitarget therapy using tacrolimus and mycophenolate mofetil (MMF) has been reported to be effective as induction therapy of Class III to Class V lupus nephritis¹. However, its efficacy on lupus nephritis presented with RPGN has not been well reported.

Objectives: We aimed to examine the efficacy of multitarget therapy on lupus nephritis presented with RPGN.

Methods: We retrospectively analyzed patients with biopsy-proven lupus nephritis, who clinically showed RPGN, and were treated by multitarget therapy with tacrolimus and MMF in our department. Data were expressed as mean $\pm$ SD.

Results: Five lupus nephritis patients (3 female) with RPGN were treated by multitarget therapy as induction therapy. Mean age was 36.6 $\pm$ 13.5 years old. Renal biopsy at treatment revealed Class IV(A) in 2, Class IV(A+C) in 1 and Class IV(A)+V in 2. The percentage of glomerular crescents was 23.1 $\pm$ 25.4%. eGFR and proteinuria at the initiation of treatment were 46.8 $\pm$ 11.5 mL/min/1.73m² and 7.7 $\pm$ 3.4 g/gCr, respectively. Patients were initially treated with methylprednisolone pulse therapy followed by 0.8-1.0 mg/kg of prednisolone (PSL), 2-3 mg/day of

tacrolimus and 1000 mg/day of MMF. At 6 months, eGFR and proteinuria improved to 72.9 $\pm$ 11.3 mL/min/1.73m² and 0.19 $\pm$ 0.13 g/gCr, respectively. At 12 months, eGFR and proteinuria further improved to 76.8 $\pm$ 7.8 mL/min/1.73m² and 0.10 $\pm$ 0.07 g/gCr, respectively and the dose of PSL was reduced to 6.6 $\pm$ 1.5 mg/day. Three patients became positive for cytomegalovirus antigenemia and were successfully treated with antiviral therapy.

Conclusion: Multitarget therapy is effective in lupus nephritis even in patients presented with RPGN.

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SAT0178

HYDROXYCHLOROQUINE CONTROLS DISEASE ACTIVITY IN SLE AND MULTIMODAL IMAGING TECHNIQUES SHOULD BE USED TO DETECT OCULAR TOXICITY

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Background: Hydroxychloroquine (HCQ) is an immunomodulatory drug that has been shown to improve disease activity in systemic lupus erythematosus (SLE). However, retinal toxicity is an important concern.

Objectives: In this study we sought to evaluate the effect of HCQ on disease activity and damage in patients with SLE in whom HCQ was discontinued due to retinal toxicity and whether it could be restarted by a detailed ophthalmologic examination.

Methods: Patients who met SLE SLICC classification criteria and were on HCQ for at least 3 years after reaching Lupus Low Disease Activity State (LLDAS) following remission induction and were followed up for at least 3 years after termination of HCQ treatment due to retinal toxicity diagnosed with visual field test were analyzed. Disease activity (LLDAS and SLEDAI-2K) and both the number and severity of flares were recorded for each patient whilst on HCQ and after cessation of treatment. All patients were examined by two experienced ophthalmologists and were assessed by computerized visual field, optical coherence tomography (OCT), fundus autofluorescence (FAF) and fundus fluorescein angiography (FFA) to further analyze toxicity.

Results: Out of 88 patients with recorded HCQ retinal toxicity in a cohort of 1500 patients with SLE, 64 patients (mean age at diagnosis 33.4 $\pm$ 10.5 (10-57); 88.5% female) with complete data and ophthalmologic re-examination results were included in the analyses. The average duration on HCQ was 122 $\pm$ 85 (39-336) months, and the mean follow-up time was 74.6 $\pm$ 48.3 (36-239) months after the drug was discontinued. Comparison of mean disease activity in the 3-year period when patients were on HCQ to 3 years post-cessation revealed a significantly lower mean SLEDAI-2K score in the former (0.89 $\pm$ 1.28 vs. 1.3 $\pm$ 1.6, $p=0.02$). The % of visits maintaining LLDAS was higher during HCQ treatment (89.7 $\pm$ 17.6 vs. 80.1 $\pm$ 23.5, $p=0.001$). There was significantly a higher frequency of flares with a dominance of mild-moderate types after HCQ was ceased (47.5 vs. 26.2%, $p=0.03$; 39.3 vs. 22.9%, $p=0.024$ respectively). There were more patients with serious flares in the post-discontinuation period but without statistical significance (13.1% vs. 4.9% $p=0.08$). Thirty-seven (60%) of patients restarted the treatment after ophthalmologic examination. Although 38 (62.3%) patients had visual field defects in the latest examination, multimodal imaging with OCT, FAF and FFA revealed that only 19 (31%) patient had typical retinal toxicity. Five patients were found to have macular atrophy due to other causes (4 age related macular degeneration and 1 vitreomacular adhesion). Since the discrimination of macular pathology would not be possible with imaging in these patients, HCQ was not prescribed. Comparison of patients with and without retinal toxicity showed that duration of HCQ use and HCQ-free time was not significantly different between patients.

Conclusion: HCQ is effective in controlling disease activity in patients with SLE and an opportunity for re-medication with HCQ is valuable. More than half of the

patients being able to restart HCQ after ophthalmologic examination in this study shows that it is important to perform multimodal imaging techniques in patients with retinal toxicity diagnosis. Since macular pathology can have a different etiologic background, an initial ophthalmologic examination is also necessary. Lack of difference in the duration of HCQ exposure and drug-free time between patients who restarted treatment and who could not may be a sign of personal sensitivity to HCQ toxicity.

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SAT0179

ADHERENCE TO HYDROXYCHLOROQUINE INFLUENCES THE INCIDENCE OF ORGAN DAMAGE DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:

Objectives: Hydroxychloroquine (HCQ) is a cornerstone drug in patients with systemic lupus erythematosus (SLE), decreasing the risk of flares and comorbidities and improving survival. This study investigated the effects of HCQ adherence on clinical manifestations, disease activity, and organ damage in Korean patients with SLE.

Methods: Data on 299 SLE patients were obtained from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, PGA, and SLEDAI-2000 and SLICC damage index scores were recorded at the time of enrollment and repeated annually for 4 consecutive years. Patients were divided into two groups according to the level of HCQ adherence. Adherence was defined by the medication possession ratio and dichotomized as $\leq 80\%$ vs. $> 80\%$. Univariate and multivariate analyses were performed to assess the impact of adherence to HCQ on clinical outcomes.

Results: Of the 299 patients, 31 (10.4%) showed poor drug adherence during the follow-up period. Patients with poor HCQ adherence were older ($P=0.011$), less insured ($P=0.024$), experienced lower employment ($P=0.033$), and had a higher rate of comorbidities such as hypertension ($P=0.048$) and depression ($P<0.001$). The non-adherent group had higher mean and changed SLICC damage index scores than the adherent group across all 4 years. In the multivariate analysis, HCQ non-adherence was significantly associated with older age (OR, 1.043; 95% CI, 1.006–1.081; $P=0.021$), depression (OR, 11.98; 95% CI, 1.099–130.6; $P=0.042$), and an annual increase in the SLICC damage index score (OR, 2.275; 95% CI, 1.369–3.779; $P=0.002$).

Conclusion: HCQ adherence might be influenced by age and depressive mood. Additionally, the poor adherence to HCQ in SLE patients was correlated with higher cumulative organ damage. Therefore, patients with SLE should be educated to take HCQ appropriately to improve their clinical outcome in clinical practice.

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SAT0180

ANTIMALARIAL DRUGS ASSOCIATED RETINOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The antimalarials remain to be the main treatment for Systemic Lupus Erythematosus (SLE). Its most important limitation when you want to increase dose or remain using them is the occurrence of retinal toxicity, which appears in a small number of patients. Since the lesions can progress even with drug withdrawal is important to perform a screening for an early diagnosis.

Objectives: To describe ocular toxicity in patients with SLE treated with antimalarials that attended the rheumatology office and to identify possible associated risk factors.

Methods: We performed a cross-sectional, retrospective study of SLE patients diagnosed of antimalarial drugs associated retinopathy, that were included in the data base of the Rheumatology department in León's Hospital between 2014-2019. Multiple clinical and therapeutic factors potentially associated with retinal toxicity were analyzed including: age, chronic kidney disease (CKD), liver failure, smoking, hypertension, Diabetes mellitus, presence of previous retinopathy, type of treatment, duration, daily dose and cumulative dose and tamoxifen intake. The diagnosis of retinopathy was performed by the Ophthalmology department. The dose of hydroxychloroquine (HCQ) used was of 400mg/day and chloroquine (CQ) 250mg/day.

Results: 437 medical records were analyzed, 20 patients diagnosed of antimalarial retinopathy were included (4.57%), 90% of them were women. The age of

diagnosis was more than 40 years in 18 patients (90%) and more than 60 years in 10 (50%) with a median of 60 years (IQR: 32,25).

The duration of treatment was ≤ 5 years in 10 patients (50%), between 6-10 years in 6 (30%), between 11-15 years in 2(10%) and between 16-20 years in 2 (10%) with a median of exposure of 5,5 years (IQR: 6,5); 15 patients (75%) were in treatment with HCQ, with CQ 2 patients (10%) and with both of them sequentially 3 patients (15%).

Of the group of patients treated with HCQ 35 % were above the global accumulated recommended dose (1000g) and 71% of them were on treatment more than 10 years. In the group treated with CQ none were above the global recommended dose (460g). Of the 3 patients that took both drugs, two were above the recommended dose for HCQ.

25% of the patients had CKD and 10% liver failure, 20% of the patients were active smokers and 15% ex-smokers.

10% of the sample had previous retinopathy related with other comorbidities (age related retinopathy and diabetes), associating hypertension and diabetes mellitus in the same percentage (15%).

Severe retinopathy was found in 1 patient (5%), mild-moderate in 9 patients (45%), retinopathy stages were not specified in 10 patients (50%).

Conclusion: In our sample we observed a prevalence of antimalarials retinopathy of 4.57%, similar of what is found in the literature. Half of the patients had retinopathy in a period of treatment ≤ 5 years, being a described risk factor the duration of treatment of more than 6 years. This early manifestation could be related to the presence of other comorbidities like hypertension, diabetes and CKD.

Dose readjustment should be considered in patients with a period of treatment of more than 10 years. Age seems to be an associated factor for the development of antimalarials retinopathy and to perform a screening in the first year of treatment is important to rule out basal disease related with more risk to develop ocular toxicity.

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SAT0181

ALTERATIONS OF PERIPHERAL LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR CHANGES AFTER OUR NEW IMMUNOREGULATORY COMBINATION THERAPIES

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by abnormal activation of circulating lymphocytes and overproduction of autoantibodies¹. Breakdown of self-tolerance is considered as a critical cause in the development of SLE². However, the quantitative changes of lymphocyte subsets in SLE are unclear. Since low-dose IL-2 and several drugs have been used to promote the proliferation of regulatory T cells (Tregs)³, we developed immunoregulatory therapies using these drugs to rebalance effector T cells with Tregs and test whether they are benefit to remission disease activity of SLE.

Objectives: To observe the different levels of peripheral lymphocyte subsets at the first laboratory examination of SLE patients with those of healthy controls (HCs) and to evaluate the effect of immunoregulatory combination therapies on levels of lymphocyte subsets in patients with SLE.

Methods: From September 2014 to December 2019, a total of 985 diagnosed patients with SLE (878 females, 107 males, mean age 42.99 ± 13.37 years) and 206 healthy adults were enrolled in this retrospective cross-sectional study. And 795 patients with SLE (711 females and 84 males, mean age 38.26 ± 15.242 years) were received the immunomodulatory drugs (IMiDs) such as low-dose interleukin-2, rapamycin, metformin, retinoic acid, coenzymes Q10 or other immunomodulatory treatments. The absolute numbers of T, B, NK, CD4⁺T, CD8⁺T, Th1, Th2, Th17 and CD4⁺CD25⁺Foxp3⁺T regulatory cells (Tregs) in peripheral blood (PB) of these individuals were measured by Flow Cytometer (FCM) combined with standard absolute counting beads.