Table 1. Estimated association between vitamin D levels and odds of organ-specific lupus disease activity, adjusting for age, race, sex, calendar year, prednisone use and plaquenil use

Vitamin D Level (ng/mL)	Immunologic Disease Activity		Skin Disease Activity		Renal Disease Activity	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
<10 (n=163)	1.0 (0.7, 1.5)	0.88	1.4 (1.0, 2.1)	0.049	3.1 (2.0, 4.9)	<0.0001
10–20 (n=1039)	1.0 (0.9, 1.1)	0.93	0.9 (0.8, 1.1)	0.41	2.2 (1.5, 3.1)	<0.0001
20–30 (n=2760)	1.0 (0.9, 1.1)	0.97	1.0 (0.9, 1.2)	0.53	1.6 (1.2, 2.0)	0.0008
30–40 (n=3959)	1.0 (0.9, 1.1)	0.78	1.1 (1.0, 1.2)	0.13	1.2 (0.9, 1.5)	0.23
40–50 (n=3578)	1.0 (Ref Grp)		1.0 (Ref Grp)		1.0 (Ref Grp)	
50–60 (n=2308)	1.0 (0.9, 1.1)	0.78	1.1 (0.9, 1.3)	0.19	1.0 (0.7, 1.3)	0.91
60–70 (n=929)	1.0 (0.9, 1.2)	0.98	1.0 (0.8, 1.3)	0.74	0.8 (0.5, 1.3)	0.33
70–80 (n=504)	1.1 (0.8, 1.2)	0.92	1.3 (1.0, 1.7)	0.072	0.8 (0.4, 1.4)	0.41
80+ (n=356)	1.1 (0.9, 1.4)	0.42	1.4 (1.0, 1.9)	0.072	0.6 (0.3, 1.6)	0.32

However, for skin activity, there was a significantly elevated risk among those in the very extreme levels of vitamin D. For Renal Disease Activity, there was a significantly higher rate of renal disease activity among those with low levels of vitamin D. In addition, there was a clear trend such that the higher the vitamin D, the lower the risk of renal disease activity. We then conducted a “within person” analysis. In this analysis, each person serves as his own control, and the question is: “When a person has a vitamin D level lower than his/her average, are they more likely to have renal disease activity”. Note, this analysis implicitly adjusts for race, sex, and all variables (measured and unmeasured) that are invariant within a person. The results are shown in Table 2.

Table 2. Within-person analysis of the relationship between vitamin D levels and renal activity adjusting for prednisone use, plaquenil use, and implicitly for all time-invariant characteristics

Vitamin D Level	Odds Ratio	P-value
10 ng/mL or more lower than personal average	1.5 (1.3, 1.8)	<0.0001
Within 10 ng/mL of the personal average	1.0 (Ref Grp)	
10 ng/mL or more higher than personal average	0.8 (0.7, 1.0)	0.080

For Renal, it appears (based on the within-person analysis), that increasing vitamin D results in a reduction in renal activity. Based on other analyses, it is clear this drop was mostly among those in the vitamin D deficiency range. **Conclusions:** Low vitamin D is associated with cutaneous and renal SLE activity, but not with immunologic (low C3 or high anti-DNA) activity, in adjusted analyses. **Disclosure of Interest:** None declared **DOI:** 10.1136/annrheumdis-2017-eular.4526

AB0462 VITAMIN D SUPPLEMENTATION SIGNIFICANTLY REDUCES CHOLESTEROL IN SLE

M. Petri¹, L.S. Magder². ¹Johns Hopkins University School of Medicine; ²University of Maryland, Baltimore, United States

Background: The benefit of vitamin D on SLE global and renal activity have now been proven by both cohort studies and a clinical trial. The benefits on cardiovascular risk factors, however, are less well understood. **Objectives:** We present the first longitudinal study on hyperlipidemia. **Methods:** A within-person analysis addressed the question of whether a person tends to have higher cholesterol when her vitamin D is lower than her average vitamin D. To assess this, for each visit, we calculated the difference between the vitamin D level at that visit and the person's average of vitamin D. Differences in the range of vitamin D <50 ng/mL were distinguished from differences in the range above 50 ng/mL. Then we modelled the relationship between these differences in vitamin D and the difference between the person's cholesterol at each visit and the person's average cholesterol. **Results:**

Table 1. Difference in Cholesterol at each visit per 10 ng/mL difference in between the patient's vitamin D at that visit and the patient's average vitamin D

Range of Vitamin D	Estimated difference in cholesterol (relative to a patient's average cholesterol) as a function of differences in a patient's Vitamin D levels (relative to her average Vitamin D levels)			
	Unadjusted	P-value	Adjusted ¹	P-value
0–50 ng/mL	-3.4 (-3.9, -2.9)	<0.0001	-3.1 (-3.6, -2.6)	<0.0001
50+ ng/mL	-1.1 (-1.7, -0.5)	0.0003	-1.0 (-1.7, -0.4)	0.0016

¹Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BM and systolic blood pressure.

Table 2. Difference in Cholesterol per 10 ng/mL Difference in Vitamin D

Range of mean Vitamin D	Estimated difference in cholesterol per 10 ng/mL difference in Vitamin D (95% CI)			
	Unadjusted	P-value	Adjusted ¹	P-value
0–50 ng/mL	-3.7 (-4.2, -3.2)	<0.0001	-3.0 (-3.5, -2.4)	<0.0001
50+ ng/mL	-0.9 (-1.5, -0.2)	0.014	-1.1 (-1.8, -0.3)	0.0037

¹Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BMI and SBP.

This means that at a particular clinic visit, if a person's vitamin D is higher than

the person's mean vitamin D by 10 ng/mL and the person has vitamin D below 40 ng/mL, then the expected cholesterol will decrease by 3.4 mg/dL. There is no significant effect of higher vitamin D among those whose mean vitamin D exceeds 50.

Conclusions: Vitamin D supplementation (in those whose level is below 40 ng/mL) has a significant benefit on total cholesterol that is independent of age, sex, ethnicity, Plaquenil, prednisone and body mass index. Vitamin D supplementation - as it also helps systolic blood pressure - is both important for SLE activity and for reduction of cardiovascular disease. **Disclosure of Interest:** None declared **DOI:** 10.1136/annrheumdis-2017-eular.1647

AB0463 THERAPEUTIC PLASMA EXCHANGE (TPE) FOR REFRACTORY SLE: A COMPARISON OF OUTCOMES BETWEEN DIFFERENT SUB-PHENOTYPES?

A. Soyuzo¹, O. Karadag², L. Kilic², T. Karaagac Akyol³, S. Apras Bilgen², O.I. Ozcebe⁴. ¹Department of Internal Medicine; ²Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine; ³Blood and Apheresis Unit, Hacettepe University Hospitals; ⁴Department of Internal Medicine, Division of Haematology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Background: Therapeutic plasma exchange (TPE) offers an alternative therapeutic modality for patients with systemic lupus erythematosus (SLE) and primary antiphospholipid syndrome (APS). However, there is conflicting evidence regarding its efficacy in different sub-phenotypes. **Objectives:** This study aims to investigate the main clinical characteristics and outcomes of patients with different phenotypes of SLE and APS treated with TPE at a tertiary care centre. **Methods:** Database of Blood and Apheresis Unit between 2001–2013 was screened for patients with SLE and primary APS. SLE disease activity index (SELENA-SLEDAI), the indications for treatment, complications and outcomes were obtained from review of medical records and phone calls. A total of 24 patients (SLE: 20, APS: 4) were recruited for the study. **Results:** Mean ages of SLE (M/F: 1/19) and primary APS (PAPS) patients (M/F: 2/2) were 32.4±12.89 and 52.0±10.7, respectively. The main indications for TPE were haematologic, neurologic, pulmonary involvement and APS-related. TPE was preferred in 8 patients because of leukopenia, and co-infection. SLEDAI was significantly decreased after TPE (16.7±8.3 vs. 8.8±3.1, p=0.001). Both primary APS and SLE related CAPS patients had completely responded to TPE. Success rate of TPE in patients with thrombocytopenia were lower than patients with haemolytic anaemia. Median (IQR 25%–75%) TPE sessions were 6.5 (5–10.5).

Table 1. Clinical, disease activity, treatment findings and TPE outcomes of SLE patients

Patient number	Major TPE indication	Age/ Sex	R/o Mphr sis	Pre-TPE Drugs	preTPE SLEDAI	Concomitant problem, synchronous treatment/procedures	PostTPE SLEDAI	Outcome	Follow-up
1	TTP	39	no	MP, CYC	13		23	CR	144 months
2	Thrombocytopenia, bleeding	59	no	MP	5		4	PR	5 months
3	Thrombocytopenia, cerebral hemorrhage	24	yes	MP, CYC, fmg	37	1, MP, HD	NA	Ectus	
4	Thrombocytopenia, bleeding	22	yes	MP, CYC	31	MP, RTX, HD	34	PR, HD	58 months
5	Thrombocytopenia, bleeding	15	no	fmg	9		9	TI	12 months
6	Renal Failure, Cytopenia	54	yes	MP, CYC, MMF	27	1, MP, CYC, HD	5	CR	33 months
7	Renal Failure	22	yes	MP, CYC, MMF, RTX, fmg	16	PR, HD	8	CR	3 months
8	Alveolar hemorrhage	30	yes	MP, CYC, fmg	16	MP, CYC, HD, MP	NA	Ectus	
9	Alveolar hemorrhage	18	yes	MP, CYC	38	MP, CYC, RTX, HD, MMF	NA	Ectus	
10	Pulmonary fibrosis, Dysaeria, Skin	33	no	MP, CYC, fmg	13	MP, CYC	7	PR, pulm HT	23 months
11	Psychosis, Active Disease	26	no	MP, CYC	23	1, MP, CYC	11	CR	48 months
12	Neuromyotonia, vision loss, paraplegia	32	no	MP, CYC, fmg	20	MP, CYC	10	CR	96 months
13	Myositis Gravis, generalized weakness	32	no	AZA	12	L	22	CR	132 months
14	Myositis Gravis, generalized weakness	30	no	fmg	11		NA	Ectus	
15	Longitudinal myelitis, quadriplegia	23	yes		29	PR, MP, CYC, RTX	10	PR, paraplegia	16 months
16	CAPS	25	no		24	MP, CYC	10	CR	84 months
17	APS widespread thromboses	60	no	MP, CYC, fmg	11		8	CR	4 months
18	Evans syndrome	33	no				9	CR	36 months
19	Hemolytic anemia	47 M	yes	MP, CYC, fmg	28	MP, CYC	NA	Shew up TPE	12 months
20	Hemolytic anemia	38	no	MP, CYC	8		3	CR	73 months

Abbreviations: L: leukopenia, PR: Pneumonia, MP: Pulse-methyl prednisolone, CYC: Cyclophosphamide, AZA: Azathioprine, RTX: Rituximab, HD: Hemodialysis, MMF: Methylmethanolate, CR: complete response, PR: partial response, TI: treatment failure

Conclusions: This study suggests catastrophic antiphospholipid syndrome (CAPS) and other APS related problems respond well to the TPE treatment. TPE should be kept in mind for the treatment of patients with other features of SLE, especially those resistant to other agents and in the presence of leukopenia and psychosis **Disclosure of Interest:** None declared **DOI:** 10.1136/annrheumdis-2017-eular.4426

AB0464 AZATHIOPRINE METABOLITES IN CONNECTIVE TISSUE DISEASE

P. Pontony, T.Y.-E. Tsai. *Rheumatology, the Canberra Hospital, Canberra, Australia*

Background: Azathioprine (AZA) is a common treatment for connective tissue diseases (CTD). AZA is a pro-drug which is metabolised to active moieties of

6-thioguanine (6-TGN) and 6-methylmercaptopurine (6-MMP). These metabolites, rather than the absolute dose of AZA, are associated with clinical efficacy and toxicity. An idiosyncratic skewed metabolism towards 6-MMP in some patients ("shunters") increases the risk of hepatotoxicity and treatment failure. Allopurinol can correct such shunts¹. Therapeutic protocols using metabolite concentrations have been shown to be cost effective, improve efficacy, and decrease treatment morbidity in IBD¹. Only one small study estimated a therapeutic 6-TGN level for SLE patients². There are scant data on AZA shunters in connective tissue disease³.

Objectives: Explore the proportion of AZA therapeutic failure, toxicity, and shunters in CTD patients.

Methods: Retrospective, multicentre audit of AZA metabolite levels in CTD patients from 2012–2016. Patient demographics, treatments, disease activity and drug toxicity were also extracted.

Results: 61 testing episodes occurred in 34 patients whose mean age was 55 (32–79) years; predominantly female (N=26, 77%), with SLE (N=19, 56%). Active disease was present in 15/61 (25%) episodes. 20/34 (60%) patients were on HCQ + AZA. 25/34 (76%) of patients were either on no or <10mg/day of prednisone. 22/61 (36%) episodes had bone marrow suppression, and 8/61 (13%) had moderate liver function derangement. 12/35 (34%) patients were AZA shunters.

Based on AZA metabolite levels, patients were classified into four categories:

Classification ³	6-TGN	6-MMP	Prevalence in Study (N)
Underdosed/ noncompliant	Low	≤ Normal	9
Appropriately dosed	Therapeutic	≥ Normal	23
Overdosed	High	≥ Normal	16
6-MMP Shunter	Low	> Normal	13

SLE patients were over-represented in the underdosed/non-compliant category (7/9). Patients in underdosed and 6-MMP shunter categories had more active disease (44% & 31%), compared with appropriate and overdosed (17% and 19% p=0.24). Surprisingly, patients who were overdosed by 6TGN levels had the lowest mean AZA dose. 6-MMP shunters had significantly lower median 6TGN levels (147pmol/8x10⁸ RBC), yet toxic MMP levels (9630pmol/8x10⁸ RBC) that was associated with worst LFT derangement prevalence (4/13, 31% vs <13%, p=0.16).

Conclusions: AZA dose is poorly predictive of 6-TGN and 6-MMP levels. Overall, one third of CTD patients were shunters, with lower 6-TGN levels and more hepatotoxicity. Only 40% of test episodes were appropriately dosed. Patients with low disease activity are more likely to have adequate 6TGN levels, however, 40% of patients with CTD won't have adequate disease control despite therapeutic 6-TGN levels. AZA metabolites can identify the multiple causes for therapeutic failure (under dosing, shunter, or true non-response), and enable early detection of shunters to avoid liver toxicity.

References:

- [1] Croyle, L., & Morand, E. F. (2015). Optimizing the use of existing therapies in lupus. *Int J Rheum Dis* 18(2), 129–37.
- [2] Askanase, AD et al (2009). Use of pharmacogenetics, enzymatic phenotyping, and metabolite monitoring to guide treatment with azathioprine in patients with systemic lupus erythematosus. *J Rheum*, 36(1), 89–95.
- [3] Haines, ML et al (2011). Clinical usefulness of therapeutic drug monitoring of thiopurines in patients with inadequately controlled inflammatory bowel disease. *Inflam Bowel Dis*, 17(6), 1301–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2405

AB0465 ASSOCIATION BETWEEN SAFETY, EFFICACY AND HYDROXYCHLOROQUINE DOSAGE IN THE TREATMENT OF CUTANEOUS LUPUS ERYTHEMATOSUS AND SYSTEMIC LUPUS ERYTHEMATOSUS

R. Wakiya, T. Kameda, M. Izumikawa, S. Nakashima, H. Shimada, H. Ozaki, A. Kondo, N. Kadowaki, H. Dobashi. *Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Kagawa University, Kagawa, Japan*

Background: Hydroxychloroquine (HCQ) are considered to be effective against cutaneous lupus erythematosus (CLE) and symptoms associated with systemic lupus erythematosus (SLE) such as rashes, joint pain, and fatigue. In a randomized controlled trial in stable active patients with SLE on HCQ treatment, those who achieved blood HCQ levels greater than or equal to 1000ng/ml had a tendency for reduced SLE flares during a 7 month period [1]. To prevent ocular toxicity, HCQ should be maintained at a dose of 6.5mg/kg or less for ideal body weight [2], however, optimal HCQ dosage is unclear.

Objectives: To extract the problem of the dosage based on ideal body weight and identify safer and more effective HCQ dosage.

Methods: We enrolled patients who took HCQ for SLE or CLE more than 3 months in our institute and 2 related facilities from September 2015. We used Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) to evaluate cutaneous symptoms and evaluated effect at start of administration and 3 months of that. The attending doctors assessed the adverse events (AEs). We investigated the change of serum biomarker, such as the value of serum

complement and anti-ds-DNA body, the number of white blood cells, lymphocytes and platelets.

Results: We enrolled the 30 patients with administration of HCQ more than 3 months and in CLE were 2 cases, in SLE were 28 cases. In 21 cases HCQ dosage were based on ideal weight. The AEs were in 13/30 cases (43.3%). The AEs were the new cutaneous symptoms in 5 cases, eye manifestation in 3 cases (abnormal visual field in 2 cases, color anomaly in 1 case), diarrhea in 2 cases, fever in 2 cases, feeling of fatigue in 2 cases, renal dysfunction in 1 case, muscular pain in 1 case, and pericarditis in 1 case. The eye manifestation in the 3 cases disappeared for a few days by stopping or reducing HCQ dosage. Although we needed glucocorticoid treatment for pericarditis, the other AEs improved by reducing HCQ dosage or stopping. The AEs of taking HCQ 200mg/day were in 6 cases, 200mg and 400mg alternatively on every other day in 6 cases, and 400mg/day in 1 case. The AEs of taking HCQ dosage based on ideal body weight were in 10/21 cases (47.6%) and by minimal dosage in 3/9 cases (33.3%). 22/28 cases (78.6%) significant improved cutaneous symptoms (amount of mean change of CLASI -4.57, p=0.024). There is no difference in the efficacy of cutaneous symptoms between group received HCQ based on ideal body weight (80.0%) and the others (92.3%). 5/21 cases of HCQ based on ideal body weight were made to reduce HCQ dosage due to AEs, but all 5 cases improved cutaneous symptoms. 53.3% (16/30) cases increased complement, but other biomarkers didn't change.

Conclusions: HCQ was effective for the treatment of CLE even when HCQ dosage was reduced due to AEs. These findings suggest that low-dose HCQ is also effective and safe, and HCQ initial dosage wasn't the need to adjust for ideal body weight.

References:

- [1] Costedoat-Chalumeau N, et al. Hydroxychloroquine in systemic lupus erythematosus: results of a French multicentre controlled trial (PLUS Study). *Ann Rheum Dis*. 2013;72(11):1786–92.
- [2] Ronald B. Melles, Michael F.Marmor. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. *JAMA Ophthalmol*. 2014;132(12):1453–60.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3928

AB0466 THE EFFECT OF OMEGA-3 FATTY ACIDS ON DISEASE ACTIVITY, ENDOTHELIAL FUNCTION, INFLAMMATORY MARKERS, AND LIPID PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED TRIALS

R. Castillo¹, P.P. Uy¹, D.M. Francisco¹, S. Lakshminarayanan². ¹Internal Medicine; ²Rheumatology, University of Connecticut, Farmington, United States

Background: Omega-3 fatty acids have been shown to have potentially beneficial immunomodulatory activity in autoimmune conditions such as rheumatoid arthritis and Sjogren's syndrome. Whether this extends to systemic lupus erythematosus (SLE) remains unclear.

Objectives: We undertook this study to summarize the body of evidence available from published clinical trials on the effectiveness of omega-3 fatty acids on clinical and laboratory outcomes in SLE.

Methods: Two independent reviewers systematically searched PubMed, MEDLINE, Scopus, and the reference lists of related articles for studies published from inception to November 2016 using relevant keywords. Randomized, controlled trials (RCTs) on SLE patients comparing omega-3 fatty acids with placebo were included in the analysis. The quality of the included RCTs was assessed in accordance with the Cochrane Handbook. A random effects model was used to pool extracted data. Heterogeneity was evaluated with Chi² test and I², with p-values <0.05 considered significant. Data presented in median and interquartile range were converted to mean and standard deviation using the method described by Wan et al.

Results: A total of seven clinical trials consisting of 303 subjects with a duration of treatment ranging from 12 to 52 weeks were included. In studies using SLAM-R as the measurement of disease activity (n=82), there was a statistically significant mean score reduction in the omega-3 fatty acid group vs. the placebo group at 24 weeks. However, in studies that used mean change in SELENA-SLEDAI (n=117, WMD: -0.87, 95% CI: -3.9, 2.17, I²=0%, p=0.58) and PGA (n=117, WMD -0.46, 95% CI: -1.16, 0.24, I²=85%, p=0.20) scores, there was no significant effect (Figure 1). Mean brachial artery diameter after 12 weeks likewise did not reveal

Figure 1. Effect of omega-3 fatty acids on SLE disease activity as measured by mean change in SELENA-SLEDAI (A) and PGA (B) scores.