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Background: There is increasing evidence for the role of vitamin D in the reduction of disease activity in SLE. The objective of this study was to compile the evidence for vitamin D supplementation in SLE patients with regards to helping develop guidelines.

Methods: The PubMed and Cochrane databases were searched ((systemic lupus erythematosus[MeSH Terms]) OR systemic lupus erythematosus[Title/Abstract]) OR lupus [MeSH]) AND ((vitamin D[MeSH Terms]) OR vitamin D[Title/Abstract]) AND (last 10 years [PDat] AND adult[MeSH] AND Humans[MeSH] AND English). A total of 190 papers that met the criteria were assessed for relevance and parameters measured, leaving 77 papers. Duplicates, case reports and papers not measuring vitamin D were removed. Final selection using the Critical Appraisal Skills Programme screening tool and again for relevance gave 32 papers. This process was reviewed and papers checked by another medical student. Papers were then graded using the Centre for Evidence-Based Medicine scale. P-values, number of patients and strength of association between vitamin D level and disease activity were extracted, as were the vitamin D levels defined as 'replete'. Papers were divided into positive (those finding a significant relationship between vitamin D and the parameter measured) and negative.

Results: A total of 32 papers were graded and results analysed. Twenty-six found that lower levels of vitamin D corresponded to higher disease activity as measured by SLEDAI (22), BILAG (1), biomarkers (8) and fatigue scores (2). Two randomized controlled trials (RCTs) met the criteria: the positive trial found SLEDAI >11 was associated with $<20 \, \text{ng/ml}$ vitamin D (P=0.033), while the negative trial measured vitamin D over 12 weeks as opposed to existing levels. It also assessed the IFN signature, which is yet to be validated as a marker for SLE activity. Of the SLEDAI measuring papers, 14 found a significant (P < 0.04) inverse correlation between SLEDAI and serum vitamin D (3925). Seventeen papers found vitamin D levels <20 ng/ml correlated with higher SLEDAI (levels 1b-2b). There is a discrepancy over the level of vitamin D considered replete. One study found a reduced SLEDAI with vitamin D < 40 nmol/l, while others saw 20 ng/ml as replete with narrow confidence intervals. Six papers quoting no relationship were grade 2b or below (205 pooled patients). Two studies looked at carotid plaque thickness and atherosclerosis in 199 patients (2b + 3b). The lack of a gold standard disease marker causes difficulty in the interpretation. Of the two studies measuring fatigue, the positive study was a stronger retrospective cohort study and found a greater negative correlation (r = -0.364). This study included 19 more patients than the negative study (r = -0.12), which was not considered significant.

Conclusion: Patients with >20 ng/ml vitamin D have lower disease activity measured by various parameters. Those with >30 ng/ml have an even greater reduction in disease activity. This is valuable evidence for the role of vitamin D supplementation in the practical management of SLE. There is a need for more RCTs and the agreement of a biomarker for disease activity.

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