Research Article

Effects of Vitamin D Supplementation and Systemic Lupus Erythematosus Disease Activity

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ABSTRACT

Background: Systemic Lupus Erythematosus (SLE) patients tend to experience vitamin D deficiency in attribution to several factors. However, studies linking vitamin D levels and SLE disease activity in children are still lacking, particularly in Indonesia.

Objective: This study aims to analyze the effects of vitamin D supplementation on the activity of SLE among children.

Methods: This was a quasi-experimental study with a pre-post treatment test design in same group. A total of 20 pediatric patients with SLE at Dr. Moewardi Hospital who met the inclusion criteria were included in the study for a period of 3 months. Vitamin D levels were measured before and after vitamin D supplementation.

Results: A total of 18 pediatric patients with SLE were included in the final analyses with an average age of 14.1 □ 2.53 years. Kidney and skin were the most commonly affected organs among the study participants. There was a significant difference in the average Mex-SLEDAI score before and after the intervention ($p = 0.006$). Vitamin D level correlated negatively with SLE disease activity prior to intervention ($r = -0.616$; $p = 0.003$). Increased vitamin D levels also correlated significantly with decreased SLE disease activity ($r = -0.493$; $p = 0.044$).

Limitations: The sample size was quite small as it was a single-center study and the subjects were not recruited in a random, double-blind fashion.

Conclusions: There is a negative correlation between vitamin D levels and SLEDAI scores. Higher levels of vitamin D shall reduce the SLEDAI scores.

Keywords: SLE, SLEDAI, vitamin D.

INTRODUCTION

Vitamin D is a steroid hormone that has a role not only in calcium metabolism and bone homeostasis but also in the regulation of immune system. Some studies suggest that 1,25-dihydroxyvitamin D contributes in controlling the immune response, in the regulation of T cells (suppression of T cell proliferation, differentiation from Th1 to Th2, inhibition of Th17 cell development and facilitation of Treg cells), inhibition of B cell proliferation and differentiation.[1-7] SLE patients tend to experience vitamin D deficiency in attribution to several factors, including avoidance of sunlight due to photosensitivity, use of sunscreen, chronic renal insufficiency, use of certain drugs such as glucocorticoids and antimalarials which can increase vitamin D clearance.[8-9]

The prevalence of vitamin D deficiency in SLE patients varies greatly in different parts of the world. In an Indonesian study comprising 81 SLE adult patients studied at Cipto Mangunkusumo Hospital in Jakarta, 33 patients experienced vitamin D insufficiency and 27 patients suffered from vitamin D deficiency. A study in the same hospital, reported 100% vitamin D deficiency in the pediatric population. Several studies in child and adult population identified a possible relationship between low vitamin D levels and increased disease activity in SLE. Other studies found no significant relationship between vitamin D and cytokine levels, the presence of anti-phospholipid syndrome, SLEDAI or SLICC, anti-dsDNA antibodies, C3 and C4.[10-17] There is currently no study

conducted to investigate the effects of vitamin D supplementation on SLE disease activity among pediatric population in Indonesia.

METHODS

This is a quasi-experimental study with one-group pre-test and post-test design (pre-post treatment test design in one group). This study was conducted at Dr. Moewardi Hospital Surakarta from July 2019 - January 2020. The samples were recruited using total sampling technique. The study was carried out after obtaining a recommendation letter for ethical approval from the Ethics Committee of Dr. Moewardi Hospital Surakarta No. 1.099/XI/HREC/2019. Parents of the study participants who agreed to participate in the study were asked provide a written consent. The subjects underwent vitamin D levels measurement as well as assessment of disease activity using SLEDAI score. Furthermore, patients with vitamin D deficiency (vitamin D levels of 0-20 ng/mL) and vitamin D insufficiency (vitamin D levels of 21-29 ng/mL) were given 2000 IU and 1000 IU vitamin D supplementation daily for a period of 3 months, respectively, while vitamin D supplementation was not given in patients with normal vitamin D levels (vitamin D levels >30 ng/mL). Repeated measurements of vitamin D levels and assessment of disease activity were performed at some point following therapy. Data is presented as mean ± SD or median (range) or proportion (percent). Univariate analysis was performed using paired student T-test and Wilcoxon test. Bivariate analysis was performed using Pearson correlation test.

RESULTS

This study was conducted in 20 pediatric patients with systemic lupus erythematosus. Three subjects passed away during the observation period prior to post-supplementation assessment and hence were excluded from the analyses.

The average age of the study participants was 14.1 ± 2.53 years, with 19 patients (95%) being female. The mean body weight was 44.2 ± 12.38 kg and the median height was 149 cm [IQR 140.5 - 152.5]. All patients received corticosteroid therapy with a mean duration of 12.7 ± 9.02 months. Skin, kidney, hematological, neuropsychiatric, endocrine and pulmonary involvement were the most commonly observed among the subjects (Table 1).

Table 1. Baseline characteristics of the study participants

Variables	Value
Age (year)	14.1 ± 2.53
Gender (% female)	19 (95%)
Weight (kg)	44.2 ± 12.38
Height (cm)	149 [140.5 – 152.5]
Duration corticosteroid therapy (months)	12.7 ± 9.02
Organ involvement	
Kidney	16 (80%)
Hematology	6 (30%)
Neuropsychiatric SLE	5 (25%)
Pulmonary	1 (5%)
Skin	17 (85%)
Endocrine	5 (25%)

At the beginning of this study, all patients experienced vitamin D deficiency with a mean vitamin D level of 10.92 ng/mL. According to the paired student T-test, a significant increase in the mean vitamin D levels were found among the study subjects before and after vitamin D supplementation ($p < 0.001$). Median SLEDAI scores also decreased with a significant mean difference ($p = 0.006$).

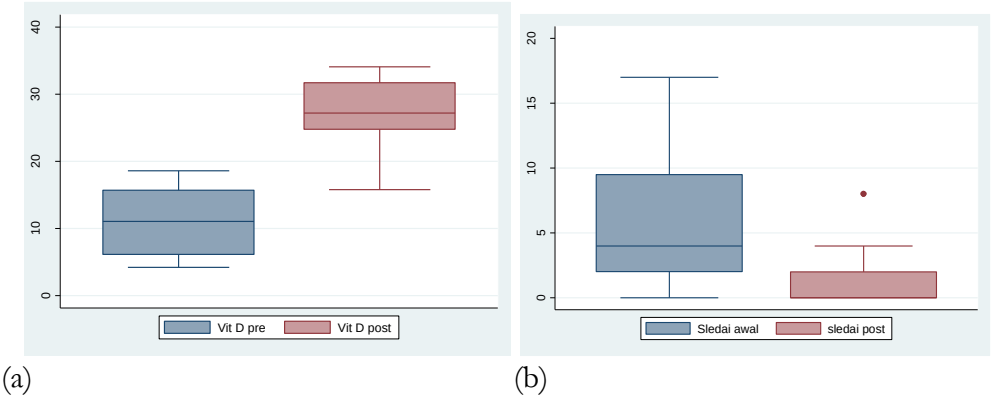

Figure 1. Box plot diagram showing the difference in the mean vitamin D levels (a) and SLEDAI score (b) between pre- and post-vitamin D supplementation period.

Table 2. The difference in the mean vitamin D levels and SLEDAI score between pre- and post-vitamin D supplementation period.

Variables (n = 17)	Value		p-value
	Pre-treatment	Post-treatment	
Vitamin D levels	11.59 ± 4.91	27.91 ± 5.51	<0.001
SLEDAI score	4 [2 – 9.5]	0 [0 – 2]	0.006

Pearson correlation test demonstrated a significant negative correlation between vitamin D levels and SLEDAI scores before therapy as well as the difference between pre- and post-treatment score ($p = 0.003$; $r = -0.616$ and $p = 0.044$; $r = -0.493$, respectively) (Table 3). Vitamin D levels following therapy also negatively correlated with SLEDAI scores but the result was not statistically significant.

Table 3. Correlation between SLEDAI score and vitamin D levels

Variables (n = 17)	r	P
SLEDAI score and baseline vitamin D levels	-0.616	0.003
SLEDAI score and post-supplementation vitamin D levels	-0.115	0.658
Difference in SLEDAI score and vitamin D levels	-0.493	0.044

DISCUSSION

SLE poses a significant risk of experiencing vitamin D deficiency in relation to various causes when compared with non-SLE population. Lin TC et al. found that the serum 25-hydroxyvitamin D levels were lower among active SLE patients compared to those with inactive SLE with $p = 0.005$. In addition, there was a significant negative correlation both in the active ($r = -0.335$; $p = 0.003$) and inactive groups ($r = -0.373$; $p = 0.016$).[18]

The mean vitamin D levels of patients initially was 11.59 ± 4.91 ng/ml; hence, all patients were considered having vitamin D deficiency. Accordingly, all patients received 2000 IU of vitamin D supplementation for a duration of 3 months. Following therapy, the patients' vitamin D levels increased with an average of 27.08 ± 4.84 ($p < 0.001$) ng/ml. Studies performed among Turkish and American children with SLE suggested that vitamin D deficiency occurs in approximately 50% and 84% of patients, respectively. While a study in Jakarta showed that all SLE patients suffered from vitamin D deficiency with an average vitamin D level of 19.3 ± 5.4 ng/ml. Another study shown after giving vitamin D 2000 IU for 3 months, found an increase in vitamin D levels from 51.1 + 33.6 nmol/l to 74 + 27.2 nmol/l [11,19,20]

The correlation test between the baseline vitamin D levels and SLEDAI scores showed a strong negative correlation with a correlation coefficient (r) of -0.58 ($p = 0.007$). It can be concluded that low vitamin D levels correlate with increased activity of SLE. The initial correlation test results between vitamin D levels and SLEDAI scores resulted in a $p = 0.003$ and a strong correlation with $r = -0.616$. In that regard, a low baseline vitamin D levels increases the activity of SLE. This finding is consistent with Eloi's study which found a significant difference between the normal vitamin D and vitamin D insufficiency groups in regard to SLEDAI

score with p = 0.001. Multicenter study conducted by Amital in 4 European countries combined child and adult population found significant negative correlation between low 5vitamin D levels and disease activity with p = 0.018; r = -0.125.[21,22]

After administering vitamin D, a negative correlation between vitamin D levels and disease activity was obtained, however, the result was not statistically significant with p = 0.658. Subsequently, further analysis was conducted to assess the correlation between pre- and post-treatment difference in vitamin D levels with the difference in SLEDAI scores. A statistically significant negative correlation was obtained (r = -0.493; p = 0.044) from the analysis.

In an Australian study conducted in a large SLE adult population, it has been shown that vitamin D deficiency is associated with higher disease activity and increased serum vitamin D level is associated with decreased disease activity over time. Stagi et al. has shown that pediatric SLE patients tend to have lower 25-(OH)-D levels than controls, and patients with active SLE have lower vitamin D levels compared to those with inactive disease. In the study conducted by Lima et al., the patients were given vitamin D supplementation for 6 months at a dose of 50,000 IU per week while the control group was given a placebo. The vitamin D baseline in this study was 19.1 ± 6.4 ng/ml in the treatment group and 19.5 ± 4.5 ng/ml in the control group. After 6 months of therapy, vitamin D levels in the treatment group increased to 31.3 ± 8.7 ng/ml, while the level in the control group was 16.5 ± 5.8 ng/ml. Changes in SLEDAI and ECLAM scores were significantly different in the two groups, with p = 0.011 for SLEDAI and p = 0.006 for ECLAM. In contrast to the study of al-Saleem et.al showing after 3 months of therapy there was a decrease in SLEDAI scores from 6 + 5.6 to 5.1 + 6.3 but not statistically significant [21-25]

Organ involvement in this study was dominated by skin and kidney involvement. Kidney involvement were mostly presented as nephritis. This is consistent with As-Saleem's study where 68% of patients experience kidney involvement. In a Turkish study, the commonly affected organ is the kidney followed by the skin.[19,25]

In this study there were no adverse effects due to vitamin D supplementation. Further research needs to be done with a larger number of samples and using the double blind randomized control trial method.

CONCLUSION

There is a significant negative correlation between vitamin D levels and SLEDAI scores. Higher levels of vitamin D shall reduce the SLEDAI scores.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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