Effect of Vitamin D Supplementation on Changes in the Severity of the Clinical Symptoms of Atopic Dermatitis

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Keywords: atopic dermatitis, vitamin D, SCORAD.

Abstract: Background: Vitamin D is a fat-soluble vitamin primarily produced by the skin, and it plays a role in innate and adaptive immune system regulation mechanisms. Vitamin D is also associated with the production of antimicrobial peptide by keratinocytes, which are potentially used for the management of atopic dermatitis, psoriasis, vitiligo, acne and rosacea. Objective: To evaluate the effect of vitamin D supplementation on changes in the severity of atopic dermatitis. Methods: This study is a double-blind clinical trial study with a parallel design. A total of 56 subjects were divided into two groups: a group that received vitamin D supplementation of 600 IU daily for 28 days (treatment group) and a group that did not receive vitamin D supplementation (control group). Both groups received standard therapy in the form of antihistamines, topical corticosteroids and moisturisers. The degree of severity of the clinical symptoms of atopic dermatitis was measured using Scoring Atopic Dermatitis index. Data analysis was conducted by using a general test linear model with a 95% confidence level. Results: The mean age of the treatment and the control group was9.5 ± 4.3 years and 7.4 ± 5.1 years, respectively. In the admissions group, the mean of 31.9 ± 9.8 improved to 12.8 ± 6.2 after 28 days of study. Similar to the treatment group, the average of the control group changed from 28.8 ± 15.1 to 13.9 ± 7.8. The result of the data analysis showed no significant difference in the degree of clinical symptom between the treatment group and the control group because the p value was equal to 0.165. Conclusion: Vitamin D supplementation of 600 IU in children for 28 days was not effective in reducing the severity of atopic dermatitis.

1 INTRODUCTION

Atopic dermatitis or atopic eczema is a chronic skin disease based on hereditary and environmental factors, and it is common in infants and children. Atopic dermatitis is a chronic inflammatory disease of the skin that occurs in 15%–25% of children and 3% of adults. Approximately 85% of patients with atopic dermatitis appear in childhood, and 70% of patients with severe atopic dermatitis develop into having rhinitis or asthma (Kim, 2012).The prevalence of dermatitis in children is 18.1% in three to five years. (Peroni, 2008)

In the last decade, vitamin D deficiency in developing countries was 30%–80% in the entire population worldwide, and prevalence was high in children aged 0–16 years. Children with asthma, atopic dermatitis, allergic rhinitis, acute urticaria and food allergies tended to be found with vitamin D deficiency. (Holick, 2008)

As children now receive very little sun exposure, many children suffer from vitamin D deficiency. Research in Jakarta found that 75.9% of children had vitamin D insufficiency and that only 15% of children had vitamin D deficiency. Several studies were conducted on children receiving vitamin D against atopic dermatitis. Research in Egypt in 2011 reported a relationship of vitamin D deficiency with the severity of atopic dermatitis. (Hartmann, 2011). Hata et al. explained that the provision of a vitamin D diet could improve the function of innate immunity of skin affected by atopic dermatitis and provedin vitro that vitamin D could stimulate the formation of antimicrobial peptide (AMP) and decrease the expression of Th2 cytokines in the body. (Hartmann, 2011). (Hata, 2014)Thus, this study aimed to evaluate the effect of vitamin D supplementation on the severity of atopic dermatitis in children.

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2 METHODS

This work is a double-blind clinical trial study with a parallel design. The subjects were composed of 56 individuals with atopic dermatitis who passed the inclusion criteria. The inclusion criteria for this study were subjects aged 1–17 years and those who did not use topical corticosteroids, oral or topical antibiotics, oral antivirals and topical calcineurin inhibitors at least oneweek before the study. The diagnosis of atopic dermatitis is made based on anamnesis and physical examination of the patient. Patients who have a history of kidney disease, kidney stones, hyperparathyroidism, sarcoidosis, tuberculosis and lymphoma and those who received systemic immunosuppressive therapy, chemotherapy, light therapy andoral calcineurin inhibitor for 30 days prior to the visit to the polyclinic were excluded as research subjects.

Subsequently, the subjects were divided into two groups: the first group comprised 25 patients who received vitamin D supplementation (treatment group), and the second group was composed of 31 patients whodid not receive vitamin D supplementation (control group). Each group received standard therapy for atopic dermatitis in the form of antihistamines, topical corticosteroids and daily moisturisers. The treatment groupreceived vitamin D supplementation of 600 IU (15 mcg), which is the recommended dietary allowance, consumed once per day for 28 days.

The degree of severity of the clinical symptoms of atopic dermatitis was measured using the Atopic Scoring Dermatitis (SCORAD) index. The SCORAD scoring results have a score range of 1–100 with the following interpretation: mild <25, moderate 25–50 and severe >50. SCORAD assessment was performed twice on each subject: the initial diagnosis and after 28 days of the study. After the research data were collected, data analysis was conducted using a general test linear model with a 95% confidence level.

3 RESULTS

A total of 56 subjects who passed the inclusion and exclusion criteria participated in the study. The treatment group consisted of 11 males and 14 females, and its mean age was 9.5 ± 4.3 years. The control group comprised 16 males and 15 females, and its average age was 7.4 ± 5.1 years. The data characteristics of the research subjects are presented in Table 1.

Table 1. Data and characteristics of the subjects

Variable	Treatment Group (%) (n = 25)	Control Group (%) (n = 31)	P value
Age			0,071*
Mean ± SD	9.5 ± 4.3	7.4 ± 5.1	
Range	2–16	1–18	
Sex			-
Male	11 (44)	16 (51.6)	
Female	14 (56)	15 (48.4)	
SCORAD 0 day			0.364**
Mean ± SD	31.9 ± 9.8	28.8 ± 15.1	
Range	17–49.9	10.2–62.4	
Mild	8 (32)	16 (51.6)	
Moderate	17 (68)	14 (45.2)	
Severe	-	1 (3.2)	
SCORAD 28 days			0.549**
Mean ± SD	12.8 ± 6.2	13.9 ± 7.8	
Range	3.3–28.6	1.7–32.5	
Mild	23 (92)	29 (93.5)	
Moderate	2 (8)	2 (6.5)	
Severe	-	-	

The severity of atopic dermatitis symptoms was measured twice using SCORAD, and it was measured at baseline (0 day) and at the end of the study (28 days). In the treatment group, the mean of 31.9 ± 9.8 improved to 12.8 ± 6.2 after 28 days of study. Similar to the treatment group, the average of thecontrol group changed from 28.8 ± 15.1 to 13.9 ± 7.8. The obtained p value was 0.165 according to the data analysis that used a general linear test model with a 95% confidence level (Table 2). The results showed no significant difference in the degree of clinical symptoms between the treatment group and the control group because the p value was> 0.05.

Table 2. Results of the general linier model test between the treatment group and the control group.

SCORAD	Vitamin D (+) mean ± SD (n = 25)	Vitamin D (-) mean ± SD (n = 31)	P value
0 day	31.9 ± 9.8	28.8 ± 15.1	0.165
28 days	12.8 ± 6.2	13.9 ± 7.8	

4 DISCUSSION

Vitamin D is a fat-soluble vitamin primarily produced by the skin. When ultraviolet B exposure occurs, 7-dehydrocholesterol is converted into vitamin D3 (cholecalciferol). Vitamin D can also be found in foods and supplements, such as vitamin D2 (ergocalciferol) and vitamin D3. The skin cannot produce vitamin D2. (Russell, 2012)

Vitamin D increases the absorption of calcium in the intestine and is associated with bone metabolism. The deficiency of this vitamin in children causes rickets.Vitamin D is also important in innate and adaptive immune system regulation. (Russell, 2012) (Reinholz, 1946)Current research data prove that vitamin D plays a role in more than 200 different gene expressions in the body. (Mesquita, 2013).

Research in the 21st century has proved that adequate vitamin D levels are associated with reduced risk of various cancers, type 1 diabetes, metabolic syndrome, cardiovascular disease, peripheral arterial disease, hypertension, chronic kidney disease, stroke, bacterial infections, rheumatoid arthritis, Crohn's disease, periodontal disease, multiple sclerosis, asthma, atopic dermatitis, muscle weakness, cognitive impairment, Alzheimer's disease, depression and premature death. Various factors are involved in the occurrence of atopic dermatitis. Thus, the current study focused on the role of vitamin D supplementation in patients with atopic dermatitis. In addition to its role in calcium homeostasis, vitamin D in various studies has been demonstrated to act as an immunomodulator and in cellular differentiation. Vitamin D is also associated with the production of antimicrobial peptides or AMP by keratinocytes.

Vitamin D and its analogues play a role in the management of atopic dermatitis, vitiligo, psoriasis, acne and rosacea. (Peroni, 2011) (Mutgi, 2013; Miller, 2011)

In 2011, Peroni etal. proved that serum 25 (OH) D levels of children with mild atopic dermatitis were higher than those of children with moderate or severe atopic dermatitis ($p < 0.05$). This finding proves that vitamin D deficiency correlates with the severity of atopic dermatitis.[10] Similarly, nutritional surveys conducted on atopic dermatitis (n = 132) and healthy individuals (n = 132) showed that the group of atopic dermatitis patients had lower vitamin D levels than the healthy group despite the fact that the vitamin D serum levels were not measured. (Solvoll, 2000)

Biologically, evidence supports the link between serum vitamin D levels and the prevalence of atopic dermatitis, especially in the severity of the disease. Vitamin D is involved in the mechanisms of innate and acquired immune system regulation. Vitamin D receptors are present in various cells, including keratinocytes and a number of cells in the immune system. (Peroni, 2011; Amestejani,2014)

A double-blind, placebo-controlled clinical trial was conducted on 30 patients with atopic dermatitis given 1,600 IU/day of vitamin D and 30 others receiving placebo. After 60 days, the group receiving vitamin D therapy showed significant improvement regardless of severity ($p < 0.05$). In the placebo group, no significant improvement was observed ($p > 0.05$). The levels of serum 25 (OH) D in the group that was given vitamin D increased significantly compared with the baseline levels ($p = 0.001$). The study concluded that vitamin D supplementation could cure atopic dermatitis. (Amestejani, 2014)

Other studies evaluated the effect of vitamins D and E supplementation on clinical manifestations of

atopic dermatitis. A total of 45 subjects were involved in this double-blind clinical trial with placebo control,and they were evaluated using SCORAD. Clinical symptoms decreased significantly after 60 days of vitamin D or E or both (p = 0.004). (Javanbakht, 2015)

Although many studies have proved the effectiveness of vitamin D supplementation in symptom improvement and in the severity of atopic dermatitis, the use of vitamin D in clinical applications remains controversial. Agnieska failed to prove the benefits of vitamin D in reducing the severity of atopic dermatitis because of the absence of significant immunologic index differences, such as the phenotypes CD3, CD4, CD8, CD19, CD4/CD8 and CD16/56; natural killer T cells, anti-CD3 human leukocyte antigen, lymphocyte percentage; eosinophils and IgE levels.[16] Similarly, the current study proved that vitamin D supplementation for 28 days in the treatment group was no more effective than that in the control group in reducing the severity of atopic dermatitis in children (p = 0.165). The researchers assumed that this finding was due to the minimal dose and the relatively short supplementation time.

5 CONCLUSIONS

According to the evaluation of the two study groups, the vitamin D supplementation of 600 IU for 28 days in the treatment group was no more effective than that in the control group in reducing the severity of clinical symptoms of atopic dermatitis in children.

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