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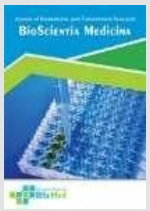

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Oral Vitamin D Supplementation as Add-On Therapy in Adult Patients with Atopic Dermatitis

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A B S T R A C T

Background: Recent studies have highlighted the possible role of vitamin D in atopic dermatitis (AD) so that it can be used as therapeutical of AD. The aim of study to evaluate the effect of vitamin D supplementation as add-on therapy in adult patients with AD. **Methods:** Twenty-four adult patients with AD were included in a randomized, double-blind, placebo-controlled trial study. This study was conducted in Dr. Moewardi General Hospital Surakarta, Indonesia, from February to March 2023. Subjects were randomly assigned to oral cholecalciferol 5,000 IU/day versus placebo for 4 weeks and all subjects were given emollient. The severity of AD was evaluated by using scoring of atopic dermatitis (SCORAD) before and after the trial. **Results:** Compared to placebo, vitamin D supplementation for 1 month obtained clinically and statistically improvement in SCORAD score compare to control (-4.508 : 4.500, p= 0.000). Moreover, vitamin D supplementation had strong negative correlation to SCORAD score after the trial (r= -0.780, p= 0,000). There were no adverse effects in either group. and **Conclusion:** Clinical improvement was achieved after vitamin D supplementation as add-on therapy in adult patients with AD.

1. Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterised by pruritus and inflamed lesions, which involves specific body areas followed by dry skin. Epidemiological studies reported that the prevalence rates of 5-20% in childhood while in adults between 3% and 5% are estimated.[1]

The exact mechanism of AD is poorly understood due to multiple factors, including genetics, environment, skin barrier disruption, immune system imbalance, and microbial dysbiosis.[2] The immune response in AD patients is biphasic; the acute phase is dominated by the T helper (Th2) response, while the chronic phase is mediated by the Th1 response. Interleukin (IL-1), IL-4, IL-3, IL13, IL-33, and IL-36 contribute to the acute process of AD, where IL-17, interferon-gamma (IFN-γ), and tumor necrosis factor-alpha (TNF-α) play an important role in chronic phase. Those cytokines correlate to the clinical manifestations of AD, which is characterized by inflamed skin lesions in the cute phase and lichenification skin in the chronic phase.[3]

The severity of AD, according to the scoring of atopic dermatitis (SCORAD), is divided into mild, moderate, and severe, with different management in each stage. A systematic review and meta-analysis study documented that patients with AD were prone to develop vitamin D deficiency compared to healthy subjects.[4] Hence, recent studies have been conducted to evaluate the efficacy of oral vitamin D in AD patients

based on SCORAD values. A previous meta-analysis study stated that the SCORAD score improved after vitamin D supplementation, suggesting its beneficial effect on AD patients.[5] Another clinical study reported the effectiveness of oral vitamin D at doses 1,600 IU/day for 12 weeks in clinical improvement of AD patients compared to control.[6] The present study aims to determine the efficacy of oral vitamin D supplementation as an add-on therapy in adult patients with AD so that it can be an optional treatment to achieve clinical improvement.

2. Methods

Study design and subject

This study was a double-blind, randomized, placebo-controlled clinical trial performed at the Dermatovenereology outpatient clinic of Dr. Moewardi General Hospital, Surakarta, Indonesia. This study was approved by the Health Research Ethical Committee of Dr. Moewardi General Hospital, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia (1363/VII/HREC/2023). This study was conducted in accordance with the Declaration of Helsinki, and the patient's confidentiality was assured.

Subjects and eligibility criteria

Subjects enrolled in the period from February to March 2023. Inclusion criteria included patients aged ≥ 18 years old, with a diagnosis of AD according to Hanifin and Radjka criteria, and willing to participate in this study by signing informed consent. Reasons for exclusion were serious skin disorder other than AD, taking systemic corticosteroids or anti-inflammatory medications, receiving oral or topical antibiotics, previous of allergic to vitamin D, pregnancy and breastfeeding, presence of active skin infection at baseline, and any known hepatic and/or renal disease.

Participants were allocated in a 1:1 ratio to receive either oral vitamin D3 5,000 IU/day or a placebo group, plus baseline therapy of urea 10% cream as emollient applied twice daily all over the body and topical corticosteroids on the inflamed skin for 4 weeks. Randomization was conducted by an observer on the day of inclusion. Treatment allocation was concealed in sequentially numbered, sealed, opaque envelopes from the patients and the investigators. At baseline, patient demographic data and clinical characteristics were collected (Figure 1).

Clinical assessment

A dermatological examination was performed on all patients to assess the AD severity based on the SCORAD score by the investigators. The disease was classified as mild (score < 25), moderate (≥ 25 to < 50) and severe (≥ 50). Re-evaluated after 4 weeks with a complete dermatological examination, including the SCORAD scores.

Statistical analysis

Categorical variables were described as numbers and percentages, and continuous variables were expressed as mean and standard deviation. The demographic characteristic data were sex, age, severity of the disease, and SCORAD score. Comparison between the two groups was made using an independent t-test, whereas the Spearman-Rho method was performed to test the correlation between numerical variables. All data were analysed using SPSS version 23, and a p-value of 0.05 was considered significant.

3. Results

The study included twenty-four subjects who were randomized, completed the study, and then included in the final analysis (Figure 1). Both groups were comparable in demographic and clinical characteristics, as summarized in Table 1. According to the independent t-test, the result showed that oral vitamin D significantly affected SCORAD values in both groups (t= 5,854, p= 0.000). The result of the Spearman-rho test obtained a significant correlation between vitamin D supplementation and SCORAD index changing in both groups (r= -0.780, p= 0.000) (Table 2).

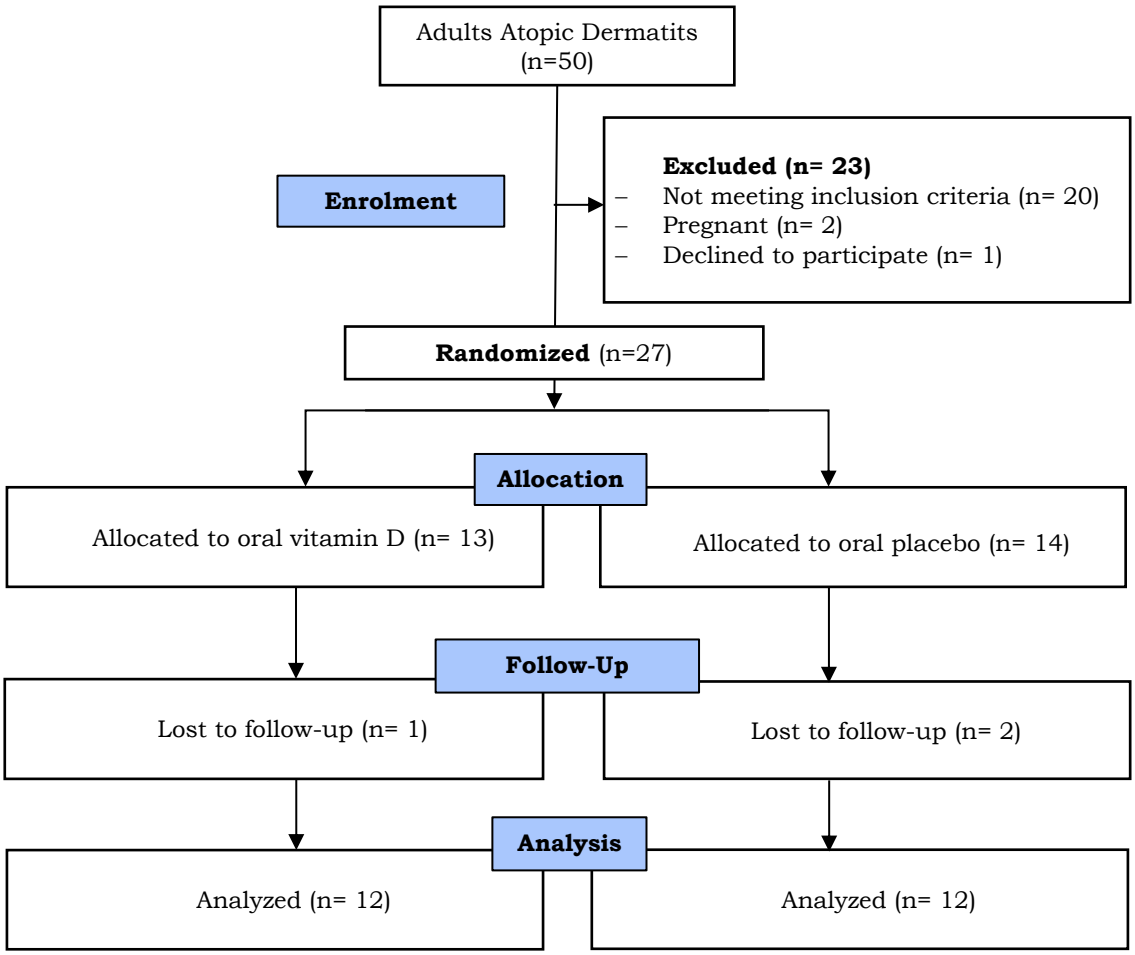

Figure 1. Research flow chart.

Table 1. Characteristics of respondent.

Variable	Treatment group n = 12 (% ; mean ± SD)	Placebo group n=12 (%; mean ± SD)	p-value
Gender			.424
Male	5 (41.67%)	7 (58.33%)	
Female	7 (58.33%)	5 (41.67%)	
Age (years)	36.66 ± 13.56	31.5 ± 13.63	.311
Severity of AD			.229
Mild	7 (58.33%)	4 (33.33%)	
Moderate	5 (41.67%)	8 (66.67%)	
Severe	0	0	
Atopic diseases			.776
AD	5 (41.67%)	5 (41.67%)	
Asthma	0	1 (8.33%)	
Allergic rhinitis	0	1 (8.33%)	
AD and asthma	1 (8.33%)	0	
None	6 (50%)	5 (41.67%)	
Clinical findings			.158
Xerotic skin	6 (50%)	4 (33.35%)	
Prurigo nodularis	2 (16.67%)	1 (8.33%)	
Lichenification	2 (16.67%)	1 (8.33%)	
Papular lichenoid	1 (8.33%)	1 (8.33%)	
Eczematous rash	0	3 (25%)	
Pompholyx	1 (8.33%)	0	
Hand eczema and lichenification	0	1 (8.33%)	
Pityriasis alba and lichenification	0	1 (8.33%)	
SCORAD index	24.35 ± 11.93	28.95 ± 12.04	.326

Abbreviation: SCORAD: scoring of atopic dermatitis.

Table 2. Effect of oral vitamin D on SCORAD index.

Variable	Vitamin D	
	T-test (n= 24)	**Correlation test (n=24)**
SCORAD	t= 5,854 p= ,000*	r= -.780 p= .000*

Abbreviation: SCORAD: scoring of atopic dermatitis
*Statistical significance with p<0.05.

4. Discussion

The prevalence of adult-onset AD showed no significant difference by gender, whereas the highest prevalence of AD was in the 25-34 years or 35-44 years age groups.[7,8] The Severity of the disease in this study was mostly mild to moderate, and none of severe AD was obtained; the most common allergic history were AD, asthma, and allergic rhinitis. Concordance to a previous study reported that a history of allergic rhinitis and asthma were observed mostly among adult patients with AD.[7] Clinical features of AD in this study include xerotic skin, prurigo nodularis, lichenification, and eczematous rash. A multicenter study reported that the most frequent AD manifestations were lichenified dermatitis, classic eczematous rash, and prurigo nodularis-like pattern.[9]

According to this study, oral vitamin D supplementation reduced the severity of AD based on SCORAD scores. This is in line with the previous study by Sanchez-Armendáriz et al., which reported the effectiveness of oral vitamin D3 5.000 IU/day as adjuvant therapy for AD, which is characterized by a decline in SCORAD scores.[10] A systematic review and meta-analysis study mentioned the efficacy of oral vitamin D in reducing SCORAD scores in AD patients. Moreover, another study also stated that high-dose vitamin D supplementation at a dose > 2,000 IU/day decreased AD severity both in adult and pediatric groups.[11,12]

Based on biological principles, vitamin D3 is recognized to have an impact on the function of the skin barrier. It regulates the structural proteins of the cornified dermis layer, which in turn affects the glycoseramides necessary for the protective lipid barrier that hydrates the skin. Through the synthesis of the anti-microbial peptides (AMPs) cathelicidin and defensin, it affects innate immunity and may reduce the incidence of skin infections.[13] Additionally, vitamin D modulates mast cells to release IL10 as an anti-inflammatory cytokine and inhibits the activity of dendritic cells as well as monocyte production via Toll-like receptors. Through lowering B cell function, it inhibits the release of immunoglobulin E (IgE) and decreases the release of proinflammatory cytokines from Th1 cells. Theoretically, these pathways could help reduce chronic inflammation in the skin followed by a decrease in SCORAD scores.[14,15]

No adverse events were reported in this study, and all subjects were satisfied with the treatment outcome. The limitations of this study were none of the severe AD patients, while the strength of this study was evaluating the effectiveness of oral vitamin D supplementation, particularly in AD extrinsic type. Further research is needed to evaluate the efficacy of oral vitamin D as an add-on therapy in adult AD patients.

5. Conclusion

Oral vitamin D supplementation was effective in reducing SCORAD scores, so it can be considered as an add-on therapy in adult AD patients without any adverse events.

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