The efficacy of vitamin D_3 supplementation in increasing 25-hydroxyvitamin D levels in childhood vitiligo patients receiving 308-nm-excimer light phototherapy

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Abstract

Vitamin D deficiency is a condition often found in various autoimmune diseases, including vitiligo. There were clinical improvements in autoimmune patients who had been given oral vitamin D supplementation, as well as vitiligo patients. This study aimed to analyze the comparison effect of a combination therapy of 308-nm-excimer light phototherapy and vitamin D_3 supplementation toward 308-nm-excimer light phototherapy alone to increase of serum 25-(OH)D levels in childhood vitiligo patients. Subjects consisted of 16 childhood vitiligo patients that divided into two groups; group I was given a combination of 308-nm-excimer light phototherapy and 5000 IU of vitamin D_3 supplement once daily, while group II was given monotherapy of excimer light. There were highly significant increase of 25-(OH)D serum in both groups which were 324.00±119.066% and 29.84±36.106%, respectively. The very significant result was seen in a comparison of average increased of serum 25-(OH)D levels between both groups. The study concluded that combination of 308-nm-excimer light phototherapy and vitamin D_3 supplementation gave a better effect than phototherapy only to increase of serum 25-(OH)D levels in childhood vitiligo patients.

Introduction

Vitiligo is an acquired depigmentation disorder resulting from progressive destruction of epidermal melanocytes,[1,2] and characterized by patches of depigmented or hypopigmented macules.[1,3] The onset of vitiligo usually in childhood or young adults. Around 25% of cases occurred before 10 years-old, while 50% of cases occurred before 20 years-old.[3,4] Vitiligo could be causing of depression in children, anxiety disorders, and disturbances of quality of life in adults.[5]

The active form of vitamin D binds to receptor vitamin D (RVD), which is widely expressed in immune cells and results from immunosuppressed effect.[6,7] *In vivo* research, 1,25-(OH)D can stimulates repigmentation of vitiligo by stimulating c-kit, microphthalmia-associated transcription (MITF), and endothelin-3 (ET3) activity in melanocytes, leading to melanogenesis.[8,9] Several uncontrolled factors may influence the increment of serum 25-(OH)D level by oral vitamin D, such as metabolism of vitamin D, sun exposure, and vitamin D rich diet.[9] Pasaribu *et al.*[10] in 2013 at Hasan Sadikin Hospital Bandung reported that from 15 adult vitiligo patients all had vitamin D deficiency. Karaguzel *et al.*[11] reported that 47% of 28 vitiligo patients in Turkey were vitamin D deficiency, whereas a similar study in children with vitiligo in Hasan Sadikin Hospital Bandung had never been done before. Finamor et al.[12] in his study of adult vitiligo patients who were given vitamin D supplements for six months reported that in 87.5% of patients, there was increased of vitamin D with 25-75% occurred repigmentation.

Based on the previous studies above, we purposed to analyze the efficacy of combination treatment of 308-excimer light phototherapy and oral vitamin D_3 5000 IU compared to monotherapy to increase of serum 25-(OH)D levels in childhood vitiligo patients.

Materials And Methods

This study was an analytic, prospective, experimental study with single-blind, randomized controlled trial design. The study included 16 childhood vitiligo patients (age <18 years old) from the Outpatient Dermatology Clinics of Hasan Sadikin Hospital, Bandung, Indonesia from January to April 2017. The exclusion criterias for this study were patients who had received oral vitamin D supplements, used corticosteroid (systemic or topical), immunomodulator (systemic or topical), phototherapy or chemophototherapy four weeks prior, or presence of other skin lesions on vitiligo patch. Subjects were divided into two groups: group 1, who received the combination of 308-nm-excimer light phototherapy twice a week and vitamin D_3 supplement 5000 IU once daily, while in group 2, received 308-nm-excimer light phototherapy only. Both groups were treated for 8 weeks. The study protocol confirmed to the ethical guidelines of Hasan Sadikin Hospital and was approved by the local ethical committee of scientific research. Prior to the research, all parents or guardian of the subject were informed about the aim of the study and gave consent. The serum 25-(OH)D level examination was done by Competitive Chemiluminescence Immunoassay (CLIA) technique using DiaSorin LIAISON® total 25-(OH)D assay. 308-nm-excimer light phototherapy was given using *Therabeam*®, while surrounding normal skin protected by sunblock SPF

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Key words: Childhood vitiligo, excimer light phototherapy, serum 25-(OH)D, vitamin D.

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45. Side effects of phototherapy such as erythema, pruritus, or blisters were recorded at each visit. The symptoms suggestive of hypercalcemia that including constipation, nausea, and vomit were also observed at each visit in subjects, who received vitamin D_3 supplementation. At 8th weeks of treatment, the serum 25(OH)D levels were reevaluated.

Results

The study participants were 16 childhood vitiligo patients in age 2 until 17 years. Group 1 consisted of nine children and group 2 consists of seven children. The characteristics of subjects are shown in Table 1.

There was a considerable difference between serum 25-(OH)D levels before and after therapy in group I ($p < 0.01$) (Table 2). The average increase of 25-(OH)D levels in group I was 290,384%, with 8 of 9 study participants in group I reaching normal 25-(OH)D levels and one participant had toxicity level. In group 2, there was a significant difference between the serum 25-(OH)D levels before and after therapy in group I ($p < 0.05$). All participants in group II had no reaching normal 25-(OH)D levels until the end of therapy. Based on Mann-Whitney statistical test results, it can be concluded that there is a statistically significant between both groups in comparison of serum 25-(OH)D levels after combination and monotherapy ($p < 0.01$).

Discussion

The main hypothesis in the pathogenesis of vitiligo is an autoimmune theory of melanocyte destruction.[1] One of the factors suspected to play a role in immunoregulation in various autoimmune diseases is vitamin D.[13] Serum 25-(OH)D is the best indicator for assessing vitamin D status, as it can describe the total vitamin D derived from diet, supplements, sunlight exposure, and vitamin D conversion from fatty deposits in the liver. Measurement of 25-(OH)D levels is easy to do, 25-(OH)D has a long half-life in circulation about two to three weeks.[13,15] Vitamin D levels before therapy in this study, was found that the deficiency occured in 6 subjects (37.5%) of study participants, insufficiency in 9 subjects (56.3%) of study participants, and 1 subjects (6.3%) had normal vitamin D level. Combination therapy of 308-nm-excimer light phototherapy and vitamin D_3 supplementation for 8 weeks provides the statistically significant improvement in serum 25-

Table 1. Characteristics of subjects.

Variable	Group		p value
	Excimer Light+Vit D N=9	Excimer Light N=7	
Age (years old)			0.363
Mean±Std	9.00±5.612	11.42±4.391	
Median	10.000	12.000	
Range (min-max)	2.00-17.00	3.00-16.00	
Gender			1.000
Male	5(55.6%)	4(57.1%)	
Female	4(44.4%)	3(42.9%)	
BMI (kg/m^2)			0.304
Mean±Std	16.78±2.193	18.60±4.499	
Median	15.970	17.360	
Range (min-max)	14.53-21.22	13.79-27.07	
Nutritional state			0.438
Underweight	0(0.0%)	1(14.3%)	
Normal	9(100.0%)	6(85.7%)	
Onset (years)			0.999
0-5	4(44.4%)	3(42.9%)	
6-10	2(22.2%)	3(42.9%)	
11-15	2(22.2%)	1(14.3%)	
16-20	1(11.1%)	0(0.0%)	
Duration (years)			1.000
0-5	8(88.9%)	5(71.4%)	
6-10	0(0.0%)	1(14.3%)	
11-15	1(11.1%)	1(14.3%)	
16-20	0(0.0%)	0(0.0%)	
25-(OH)D level before therapy			1.000
Deficiency	3(33.3%)	3(42.9%)	
Insuficiency	5(55.6%)	4(57.1%)	
Suficiency	1(11.1%)	0(0.0%)	
Toxicity	0(0.0%)	0(0.0%)	
History of therapy		0.358	
Yes	4(44.4%)	5(71.4%)	
No	5(55.6%)	2(28.6%)	
Family history			1.000
Yes	0(0.0%)	0(0.0%)	
No	9(100.0%)	7(100.0%)	
Type of vitiligo			0.990
Focal	2(22.2%)	0(0.0%)	
Segmental	1(11.1%)	1(14.3%)	
Non Segmental	6(66.7%)	6(85.7%)	

Table 2. Comparison of increment 25-(OH)D between group I and group II.

Variable	Group		p value
	Excimer Light +Vit D N=9	Excimer Light N=7	
25-(OH)D level before therapy			0.593
Mean±Std	17.08±7.903	15.00±7.096	
Median	15.500	15.100	
Range (min-max)	9.10-30.60	6.60-24.80	
25-(OH)D level after therapy			0.000**
Mean±Std	68.11±29.535	17.90±5.906	
Median	56.700	20.100	
Range (min-max)	45.00-134.00	9.50-24.80	
Δ 25-(OH)D level (%)			0.000**
Mean±Std	324.00±119.066	29.84±36.106	
Median	290.384	19.697	
Range (min-max)	200.00-509.68	-4.29-103.03	

(OH)D levels. 25-(OH)D levels before and after the combination of excimer light and vitamin D_3 phototherapy showed that the combination of excimer light and vitamin D_3 phototherapy can significantly increase the levels of 25-(OH)D ($p < 0.01$) in childhood vitiligo.The mechanism of action of vitamin D in vitiligo is still uncertainty, $1,25(OH)_2D_3$ is thought to prevent melanocyte damage and activate melanocytes by increasing the immune response, inhibiting apoptosis, oxidative, and produce some cytokines.[15]

Conclusions

Vitamin D_3 and 308-nm-excimer light phototherapy gave better efficacy than monotherapy to increase 25-OH(D) levels in childhood vitiligo patients.

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