The effect of combination narrowband ultraviolet B phototherapy and vitamin D_3 supplementation to increase serum 25-(OH)D levels in adult vitiligo patients

Reiva Farah Dwiyana, Fatima Aulia Khairani, Pusfana Meidelia, Unwati Sugiri, Reti Hindritiani, Hendra Gunawan, Oki Suwarsa

Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran - Dr. Hasan Sadikin Hospital, Bandung, West Java, Indonesia

Abstract

Vitiligo is an acquired depigmentation disorder with exact etiology is not yet known. Autoimmune hypothesis plays an important role in the mechanism of vitiligo and has been related to lower levels of 25-hydroxyvitamin D (25-(OH)D). This study aimed to analyze the comparison effect of combination therapy of NB-UVB phototherapy and vitamin D_3 supplement toward NB-UVB phototherapy alone to increase of serum 25-(OH)D levels in vitiligo patients. Subjects consisted of 24 adult vitiligo patients: group I was given a combination of NB-UVB phototherapy and 5000 IU vitamin D_3 once daily; while group II was given monotherapy of NB-UVB. There was a very significant increase of serum 25-(OH)D level in group I with an average increase was 288.65%, while group II showed a significant increase of serum 25-(OH)D serum with an average increase was 33.63%. The very significant result was seen between both groups. None of the subjects showed signs of vitamin D toxicities during treatment. The study concluded that combination of NB-UVB phototherapy and vitamin D_3 supplementation gave a better effect to increase of serum 25-(OH)D levels in adult vitiligo patients.

Introduction

Vitiligo is a skin disorder characterized by depigmentation macules caused by selective loss of melanocytes, with varying responses to therapies.[1] The pathogenesis of vitiligo is complex with interaction of multiple factors, however, the exact mechanism is not yet known.[2] The autoimmune mediated destruction of melanocytes is well accepted and has been the most prominent hypothesis in vitiligo pathogenesis. The immune reactions can be mediated by cellular immunity, humoral immunity, and action of cytokines.[3]

Vitiligo has been related with reduced vitamin D levels. Deficiency of vitamin D was suggested as a trigger for autoimmunity,[4] therefore the supplementation of vitamin D can probably be used as a treatment for vitiligo.[5] The synthesis of vitamin D occurs in epidermis from the precursor molecule 7-dehydrocholesterol (provitamin D_3) to previtamin D_3 by ultraviolet B (UVB) radiation. Previtamin D_3 next converted into vitamin D_3 (cholecalciferol) through spontaneous, temperature-dependent isomerization. Once in the circulation, vitamin D is transformed into 25-hydroxyvitamin D (25-(OH)D) by hepatic hydroxylase enzyme.[6] The circulating 25-(OH)D level is an indicator of the vitamin D status,[7] which is the best available clinical marker for diagnosis of vitamin D deficiency.[8] According to Beheshti *et al.*,[9] serum vitamin D level in patients with autoimmune disease should be assessed, and if there is a lack, the patients should be treated. Vitamin D intake and effective sun exposure are the major determinants of the serum 25-(OH)D level.[6, 8] The starting level of 25-(OH)D level influences the increment in serum 25-(OH)D in response to a given dose of vitamin D_3,[8] therefore serum 25-(OH)D measurement is needed after treatment of oral vitamin D.

Phototherapy is one of the best known and documented treatment options in vitiligo. Narrowband ultraviolet (NB-UVB) has been the effective and safe therapy for vitiligo.[10] Previous study showed that vitiligo patients receiving NB-UVB phototherapy had increase in serum 25-(OH)D levels.[11] However, based on our knowledge, there still no data about the influence of vitamin D supplementation on NB-UVB phototherapy as a long-known proven treatment in vitiligo.

According to the previous studies above, we aimed to analyze the advantages of combination treatment of NB-UVB phototherapy and oral vitamin D_3 5000 IU compared to NB-UVB phototherapy alone to increase serum 25-(OH)D levels in adult vitiligo patients.

Materials and Methods

This study was an analytical, prospective, experimental study with blocked randomized controlled trial. The subjects consisted of 24 patients (≥ 18 years old) of non-segmental vitiligo from Dermatology Clinics of Dr. Hasan Sadikin Hospital, Bandung, Indonesia. Thirteen patients received combination of 301-nm NB-UVB phototherapy twice a week and oral vitamin D_3 5000 IU once daily for 8 weeks (group I), while 11 patients received NB-UVB phototherapy alone for eight weeks (group II). Baseline serum 25-(OH)D level (week 0) were measured by Competitive Chemiluminescence Immunoassay (CLIA) technique using DiaSorin LIAISON® total 25-(OH)D assay. Patients with serum 25-(OH)D less than normal (< 30 ng/mL) were included in this study. The exclusion criterias included patients who were treated with phototherapy or immunomodulator within 4 weeks, received topical corticosteroids or vitamin D in the last two weeks, and systemic corticosteroids or vitamin D in the last six weeks. Patients with history of photosensitivity and skin malignancy were not included in this study. The study protocol conformed to the ethical guidelines of Dr. Hasan Sadikin Hospital and was approved by the local ethical committee of scientific research. After 8th weeks of therapy, serum 25-(OH)D level were re-measured in each patients.

Correspondence: Fatima Aulia Khairani, Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran - Dr. Hasan Sadikin Hospital, Bandung 40161 Indonesia.
Tel.: +62222032426 ext. 3449.
E-mail: fatimaaulia86@gmail.com

Acknowledgments: The authors would like to extend our gratitude to the staff of the Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran who contributed to this work.

Key words: NB-UVB phototherapy, serum 25-(OH)D, vitamin D, vitiligo.

Contributions: All the authors contributed equally.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: None

Received for publication: 1 February 2019.
Accepted for publication: 12 February 2019.

Dermatology Reports 2019; 11(s1):8043
doi:10.4081/dr.2019.8043

Results

This study included 24 adult vitiligo patients, consisted of 10 males (41.7%) and 14 females (58.3%). Most patients in our study were adults, with range of age were 25-64 years old, and most patients had history of topical therapy (45.8%). The characteristics of subjects are shown in Table 1.

The mean 25-(OH)D level before therapy in group I was 11.29±4.500 ng/ml, while in group II was 13.04±4.830 ng/ml. After treatment there was a very significant increase of serum 25-(OH)D level in group I by mean level was 37.88±9.958 ng/ml with average increase was 288.65% ($p = 0.001$) (Table 2). 10 of 13 subjects (76.92%) had normal serum 25-(OH)D after treatment. Group II showed significant increase of 25-(OH)D serum by mean level was 16.26±4.899 ng/ml with average increase was 33.63% ($p < 0.05$) (Table 2), but no subject had normal 25-(OH)D after treatment. Interestingly, three patients in group II had decrement of serum 25-(OH)D levels after receiving phototherapy. Very significant result ($p = 0.000$*) was seen in comparison of average increase of serum 25-(OH)D levels between both groups (Table 3). None of subjects showed symptoms of vitamin D toxicities during treatment.

Discussion

Our data showed that combination treatment of NB-UVB phototherapy and vitamin D_3 supplement gave a better effect than monotherapy of NB-UVB phototherapy to increase serum 25-(OH)D levels in adult vitiligo patients. The previous study by Sehrawat *et al.*[4] revealed that serum (25-(OH)D) levels increased in vitiligo patients after 12 weeks of NB-UVB treatment with moderate correlation. They also found that serum 25-(OH)D levels increased significantly with increase in the cumulative dose of NB-UVB. Our data also showed significant improvement of serum 25-(OH)D levels after receiving NB-UVB phototherapy for eight weeks. To the best of our knowledge, this was the first study examining the comparison effect of combination therapy of NB-UVB phototherapy and vitamin D_3 supplementation toward NB-UVB phototherapy alone to increase serum 25-(OH)D levels in adult vitiligo patients. Similar study was done by Ala-Houhala *et al.*[12] that gave NB-UVB treatment in 12 psoriasis patients who were supplemented with oral cholecalciferol 20 µg daily. They found that NB-UVB treatment significantly increased serum 25-(OH)D level in patients with psoriasis who were taking oral vitamin D supplementation, with concentration of serum 25-(OH)D remained below the toxicity level. Meanwhile, Finamor *et al.*[13] in their previous study showed that oral vitamin D_3 35,000 IU once daily for six month could significantly increase vitamin D levels in vitiligo patients. We gave oral vitamin D_3 5000 IU in our study based on the recommendations for management of vitamin D deficiency that high dosage of vitamin D as 3000-5000 IU daily for 6-12 weeks can

Table 1. Characteristics of subjects.

Variable	Group I (NB-UVB+Vit D) n = 13	Group II (NB-UVB) n = 11	Total	p value (n = 24)
Gender				0.239
Male	4 (30.8%)	6 (54.5%)	10 (41.7%)	
Female	9 (69.3%)	5 (45.5%)	14 (58.3%)	
Age (years old)				0.786
19 – 24	3 (23.1%)	1 (9.1%)	4 (16.7%)	
25 – 44	5 (38.5%)	4 (36.4%)	9 (37.5%)	
45 – 64	4 (30.8%)	5 (45.5%)	9 (37.5%)	
≥ 65	1 (7.7%)	1 (9.1%)	2 (8.3%)	
Mean ± SD	39.61 ± 15.91	45.72 ± 14.41	42.41 ± 15.23	
Type of vitiligo				0.275
Acrofacial	0 (0.0%)	1 (9.1%)	1 (4.2%)	
Focal	0 (0.0%)	1 (9.1%)	1 (4.2%)	
Vulgaris	13 (100.0%)	9 (81.8%)	22 (91.6%)	
Occupation			0.108	
Indoor job	13 (100.0%)	9 (81.8%)	22 (91.7%)	
Outdoor job	0 (0.0%)	2 (18.2%)	2 (8.3%)	
History of therapy				0.648
None	2 (15.4%)	1 (9.1%)	3 (12.5%)	
Topical	7 (53.8%)	4 (36.4%)	11 (45.8%)	
Systemic	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Phototherapy	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Topical and systemic	1 (7.7%)	3 (27.3%)	4 (16.7%)	
Topical and phototherapy	1 (7.7%)	2 (18.2%)	3 (12.5%)	
Systemic and phototherapy	1 (7.7%)	1 (9.1%)	2 (8.3%)	
Topical, systemic, and phototherapy	1 (7.7%)	0 (0.0%)	1 (4.2%)	

Table 2. Serum 25-(OH)D level before and after treatment in both group.

Variable	Group I NB-UVB + Vit D	P value	Group II NB-UVB	p value
25-(OH)D level before therapy		0.001**		0.039*
Mean±SD	11.29±4.500		13.04±4.830	
Median	10.200		10.900	
Range	5.40-20.00		6.00-21.70	
25-(OH)D level after therapy				
Mean±SD	37.88±9.958		16.26±4.899	
Median	38.000		14.400	
Range	28.60-64.20		7.20-24.70	

Table 3. Comparison of increment 25-(OH)D levels between group I and group II.

Variable	Group I (NB-UVB + Vit D)	Group II (NB-UVB)	p value
Increment of 25-(OH)D levels (%)			0.000**
Mean±SD	288.65±196.879	33.63±45.945	
Median	273.530	30.280	
Range	67.50-842.59	-31.43-131.67	

be used to replete body stores.[14] Therefore, based on the findings of our study, we may conclude that NB-UVB phototherapy and vitamin D_3 supplement gave better effect to increase serum 25-(OH)D levels in adult vitiligo patients. All these data add further beneficial role to oral vitamin D as an inducer of synthesis vitamin D in patients who received phototherapy. Miliken *et al.*[15] in their study explained that NB-UVB increases circulating regulatory T-cell (Treg) numbers, as vitamin D status is a key determinant of Treg numbers. Their findings had significant implications on the functions of phototherapy and vitamin D supplementation in prevention or treatment of autoimmune diseases. According to our findings, oral vitamin D may become choice of treatment for vitiligo in the future. Vitamin D measurement is important for screening deficiency of vitamin D in patients of autoimmune diseases, including vitiligo. The safety of oral vitamin D and its advantageous effects provide enthusiasm that improving vitamin D levels will give better outcomes in vitiligo patients.[4] However, sun exposure and daily activities were not controlled in our study, consequently became this study limitations.

Conclusions

Combination treatment of NB-UVB phototherapy and vitamin D_3 supplement gave better effect than phototherapy alone to increase serum 25-(OH)D levels in adult vitiligo patients.

References

1. Alikhan A, Daly M, Petronic-Rosic V. Vitiligo: A comprehensive review. J Am Acad Dermatol. 2011;65:473-91.
2. Boissy RE, Dell'Anna ML, Picardo M. On the pathophysiology of vitiligo: possible treatment options. Indian J Dermatol Venereol Leprol. 2012;78:24-9.
3. Mohammed GF, Gomaa AH, Al-Dhubaibi MS. Highlights in pathogenesis of vitiligo. WJCC. 2015;3(3):221-30.
4. Saleh HM, Fattah NS, Hamzah HT. Evaluation of serum 25-hydroxyvitamin D levels in vitiligo patients with and without autoimmune diseases. Photodermatol Photoimmunol Photomed. 2013;29:34-40.
5. AlGhamdi K, Kumar A, Moussa N. The role of vitamin D in melanogenesis with an emphasis on vitiligo. Indian J Dermatol Venereol Leprol. 2013;79:750-8.
6. Mostafa WZ, Hegazy RA. Vitamin D and the skin: focus on a complex relationship a review. J Adv Res. 2015;6:793-804.
7. Delvin E, Souberbielle J, Viard J, Salle B. Role of vitamin D in acquired immune and autoimmune diseases. Crit Rev Clin Lab Sci. 2014;51(4):232-47.
8. Dawson-Hughes D, Mithal A, Bonjour JP, et al. IOF position statement: vitamin D recommendations for older adults. Osteoporos Int. 2010;4:1-4.
9. Beheshti A, Ghadami H, Barikani A, Maouchehri FH. Assessment of vitamin D plasma levels in patients with vitiligo vulgaris. Acta Medica Iranica. 2014;52(2):601-6.
10. Kumar K, Rao GR, Gopal KV, Shanti G, Rao KV. Evaluation of narrow-band UVB phototherapy in 150 Evaluation of narrow-band UVB phototherapy in 150 patients with vitiligo. Indian J Dermatol Venereol Leprol. 2009;75:162-6.
11. Sehrawat M, Arora TC, Chauhan A, et al. Correlation of vitamin D levels with pigmentation in vitiligo patients treated with NBUVB therapy. ISRN Dermatology. 2014;1:1-6.
12. Ala-Houhala MJ, Karpinen T, Vähävihu K, Kautiainens H YD. Narrow-band ultraviolet b treatment boosts serum 25-hydroxyvitamin d in patients with psoriasis on oral vitamin d supplementation. Acta Derm Venereol. 2014;94:146-51.
13. Finamor DC, Coimbra RS, Neves LC, et al. A pilot study assessing the effect of prolonged administration of high daily doses of vitamin D on the clinical course of vitiligo and psoriasis. Dermatoendocrinol. 2013;5(1):222-34.
14. Diamond TH, Eisman JA, Masn RS, et al. Vitamin D and adult bone health in australia and new zealand: a position statement. MJA. 2005;182(6):281-5.
15. Milliken SV, Wassal H, Lewis BJ, et al. Effects of ultraviolet light on human serum 25-hydroxyvitamin D and systemic immune function. J Allergy Clin Immunol. 2012;129:1554-61.