Characteristics and decreased Vitiligo Area Scoring Index of vitiligo patients with narrowband-UVB phototherapy in Yogyakarta, Indonesia

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Abstract

Narrowband ultraviolet-B (NB-UVB) phototherapy is the mainstay of vitiligo therapy. The response can be evaluated using the vitiligo area scoring index (VASI) and repigmentation grade. However, few studies used VASI to evaluate phototherapy response and there are no definitive data on the reduction of VASI. This retrospective descriptive study aimed to determine the characteristics and decrease of VASI in patients with vitiligo after 36 and 48 sessions of NB-UVB phototherapy, conducted at Dr. Sardjito General Hospital, Yogyakarta, from December 2021-June 2022. The most common predilection was on the face (71.43%) and acral (61.90%). The most common responses after 36 and 48 phototherapy sessions were minimally improved (decrease in VASI<10%) and improved (reduction in VASI 10-25%). The mean decrease in VASI was 18% and 22% after 36 and 48 phototherapy sessions, respectively. 9.52% and 6.67% of patients experienced a reduction in VASI >50% after 36 and 48 phototherapy sessions, respectively. VASI assessment can be used to evaluate the response to phototherapy in vitiligo. However, VASI cannot show a reduction in vitiligo with slight repigmentation in slow-response patients.

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Key words: vitiligo, phototherapy, narrowband ultraviolet B, vitiligo area scoring index.

Contributions: NKP, concept and design of the study, writing and drafting the paper, analyzing and interpreting the data; VR, analyzed and interpreted the data; RD, concept and design of the study, drafting the work or revising it critically for important academic content; AB, concept and design of the study, drafting the work or revising it critically for important academic content. All authors gave final approval of the version of the manuscript to be published.

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

Ethics approval and consent to participate: obtained from the Medical and Health Research Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada (KE/FK/1621/EC/2022).

Availability of data and materials: data and materials are available by the authors.

Acknowledgments: the authors want to thank the staff at Klinik Bahasa, Office of Research and Publication, Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada, who kindly provided proofreading assistance.

Received: 8 March 2023.
Accepted: 23 April 2023.
Early view: 22 May 2023.

Licensee PAGEPress, Italy
Dermatology Reports 2023; 15:9708
doi:10.4081/dr.2023.9708

Introduction

Vitiligo is an autoimmune disease that causes progressive loss of melanocytes which can lead to skin depigmentation. The diagnosis is made clinically by hypopigmented macules and patches to well-defined depigmentation.[1] The prevalence of vitiligo is estimated to be 0.4-2% in the world population.[2] The psychosocial burden remains one of the problems of this disease which has an impact on decreasing the patient's quality of life.[1] However, there are no actual data regarding the incidence of vitiligo and response to therapy in Indonesia.

Vitiligo therapy is determined based on the disease activity and the extent of the lesions. Phototherapy with narrowband ultraviolet B (NB-UVB) is the first line of treatment for vitiligo patients with a lesion area >5% of body surface area (BSA).[1] The study of Liu et al. stated that NB-UVB phototherapy can still be given as early as possible, even in limited lesions, with effective results.[3] NB-UVB phototherapy will cause repigmentation and stabilization of skin lesions with minimal side effects.[1]

Evaluation of therapy is needed to determine the response to phototherapy in patients with vitiligo. The vitiligo area scoring index (VASI) was introduced by Hamzavi *et al.*[4] as a measuring tool to evaluate therapy. The Vitiligo Working Group Phototherapy recommends assessing response to treatment after 18-36 sessions with a minimum of 48 sessions to determine the lack of response to vitiligo therapy. Treatment failure was defined as lacking pigmentation after 48 or 72 phototherapy sessions.[5] However, only a few studies have used VASI to evaluate response to therapy at various specific periods.

This study aimed to describe the characteristics and evaluate VASI in patients with vitiligo treated with NB-UVB phototherapy as an indicator of response to therapy in Yogyakarta, Indonesia.

Materials and Methods

This retrospective descriptive study used patient registry data at the Dermatology and Venereology outpatient clinic, Dr. Sardjito General Hospital Yogyakarta, Indonesia, from December 2021-June 2022. Register data were used to evaluate age, gender, predilection, type of phototherapy, and VASI. Patients with vitiligo were classified into vitiligo vulgaris, segmental, focal, and acral. The decrease in VASI was assessed through registry data and patient photographic documentation at baseline before phototherapy, 36th session, and 48th session after phototherapy with NB-UVB. Inclusion criteria were vitiligo patients who underwent NB-UVB phototherapy for at least 36 sessions. Phototherapy was done 2-3 times a week. Patients who missed phototherapy for over three weeks were excluded from this study. Ethical clearance was obtained from the Medical and Health Research Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada.

Results

Forty-six vitiligo patients received phototherapy from December 2021 to June 2022. Five patients were excluded from using excimer lamp therapy. Eleven patients discontinued phototherapy for personal reasons, and eight patients had just started phototherapy and were therefore excluded from this study. There was a total of 23 patients with vitiligo received at least 36 sessions of NB-UVB phototherapy during the study period. Out of these 23 patients, one was excluded due to incomplete data, and one was excluded because of missing phototherapy for more than three weeks. A total of 21 patients with vitiligo underwent 36 sessions of NB-UVB phototherapy and 15 patients underwent phototherapy for up to 48 sessions during the study period. Of the total patients, 61.90% of patients with vitiligo were female and 38.10% were male. The most common predilection was in the face (71.43%), followed by acral (61.90%), arms (57.14%), trunk (47.62%), legs (47.62%), and neck (14.13%). 29%). In our study, vitiligo occurred in the age range of 5-54 years with an average of 25.48+14.01 years. Patient characteristics can be seen in Table 1.

The diagnosis of vitiligo is classified based on its type into vitiligo vulgaris, segmental vitiligo, focal vitiligo, and acral vitiligo. Vitiligo vulgaris was the most common diagnosis (76.19%). 66.67% of patients with vitiligo were given NB-UVB whole-body phototherapy, 28.57% received NB-UVB hand and foot phototherapy, and 4.76% received targeted NB-UVB phototherapy. 47.62% of patients were given a combination treatment with topical therapy, such as 1% pimecrolimus cream, 0.03% tacrolimus ointment, 0.1% mometasone furoate cream, and topical antioxidants. VASI observations were done at the initial session before phototherapy, the 36th session, and the 48th session after phototherapy (Table 2). Our study's mean initial VASI, VASI-36, and VASI-48 were 5.15±8.80, 4.22±6.23, and 4.06±5.59, respectively. These results indicate a decrease in VASI after 36 and 48 sessions of NB-UVB phototherapy, as shown in Figure 1. The mean reduction in VASI after 36 phototherapy sessions was 18%, with the highest decrease in VASI being 66.25%. There were four patients with vitiligo with unchanged VASI. However, there was still some repigmentation. After 48 sessions, the average decrease in VASI was 22%, with the highest reduction in VASI being 62.5%. One patient's VASI did not change after 48 phototherapy sessions. However, repigmentation was still found in a few lesions in response to therapy. Of the total 21 patients with vitiligo, 11 patients were given monotherapy using NB-UVB phototherapy, and ten patients using a combination of NB-UVB phototherapy and topical therapy. Vitiligo patients with monotherapy and combination topical therapy had a decrease in VASI of up to 25%, the most significant reduction in VASI after 36 phototherapy sessions (Table 3). At the 36th session after phototherapy, the percentage reduction in VASI was <10%, 10-25%, >25-50%, and >50% in 38.10%, 33.33%, 19.05%, and 9.52% of all patients. In the 48th session after phototherapy, the percentage reduction in VASI was <10%, 10-25%, >25-50%, and >50% in 33.33%, 33.33%, 26.66%, and 6.67% of all patients. VASI did not change in 19.05% and 6.67% of patients after 36 and 48 phototherapy sessions, respectively, but repigmentation was still found in a small number of lesions.

Table 1. Baseline characteristics of vitiligo patients.

Characteristics	N (%)
Age, min-max (median) years*	5-54 (22)
Gender	
Male	8 (38.10)
Female	13 (61.90)
Predilections	
Face	15 (71.43)
Neck	3 (14.29)
Body	10 (47.62)
Arm	12 (57.14)
Leg	10 (47.62)
Acral	13 (61.90)
Vitiligo	
Vitiligo vulgaris	21 (100)
Segmental vitiligo	16 (76.19)
Focal vitiligo	3 (14.29)
Acral vitiligo	1 (4.76)
Type of phototherapy	
Whole body	14 (66.67)
Hand and foot	1 (4.76)
Targeted	6 (28.57)
Topical therapy	
Without topical therapy	11 (52.38)
With topical therapy	10 (47.62)

SD, standard deviation; min-max, minimum-maximum. *Mean ± standard deviation: 25.48±14.01.

Table 2. Overview of changes in vitiligo area scoring index of vitiligo patients with NB-UVB phototherapy.

Observations	N	Mean ± SD	ΔVASI	%ΔVASI, mean (min-max)
Initial	21	5.15±8.80		
36 sessions	21	4.22±6.23	0.94	18 (0-66.25)
48 sessions	15	4.06±5.59	1.09	22 (0-62.50)

SD, standard deviation; min-max, minimum-maximum; VASI, vitiligo area scoring index.

Discussion

Vitiligo is a chronic autoimmune disease associated with skin pigmentation. Clinical symptoms range from hypopigmented macules and patches to well-defined and regular depigmentation, which may accompany the Köebner phenomenon, confetti-like depigmentation, or trichrome lesions. Areas of hair can be involved, which is known as poliosis. The pathophysiology of this disease is still unclear, but it is thought to be influenced by genetic predisposition, autoimmune, and environmental factors.[1,6]

Vitiligo can affect various ages, but 70-80% of cases occur before the age of 30 years.[7] The epidemiological study of Mahajan

Figure 1. Decreased VASI in vitiligo patients with NB-UVB phototherapy. **a**) initial session before phototherapy; **b**) 36th session after phototherapy; **c**) 48th session after phototherapy.

Table 3. Percentage decrease in vitiligo area scoring index of vitiligo patients with monotherapy and combination therapy.

Observations	N (%)	VASI decrease, n (%)			
		<10%	10-25%	>25-50%	>50%
NB-UVB phototherapy					
Sesi-36	11 (52.38)	3 (27.27)	5 (45.45)	2 (18.18)	1 (9.09)
Sesi-48	8 (53.33)	3 (37.50)	3 (37.50)	2 (25.00)	0 (0.00)
NB-UVB phototherapy with topical therapy*					
Sesi-36	10 (47.62)	5 (50.00)	2 (20.00)	2 (20.00)	1 (10.00)
Sesi-48	7 (46.67)	2 (28.57)	2 (28.57)	2 (28.57)	1 (14.29)
Total					
Sesi-36	21 (100)	8 (38.10)	7 (33.33)	4 (19.05)	2 (9.52)
Sesi-48	15 (100)	5 (33.33)	5 (33.33)	4 (26.66)	1 (6.67)

*Topical therapy with pimecrolimus 1%, tacrolimus 0.03%, mometasone furoate 0.1%, or topical antioxidants); VASI, vitiligo area scoring index.

et al. stated that the incidence of vitiligo varied from 2 to 83 years, with a mean age of 24.4 years.[8] In a previous study, from 945 patients, the highest incidence of vitiligo occurred at the age of <20 years (50.6%), and 26.2% occurred at the age of <12 years.[8] The age characteristics are similar to our study, which shows that age varies from age 5-54 years old, with a mean age of 25.48±14.01 years. Women and men have the same disease risk, although more female patients seek medical therapy.[1] There were 47.5% male and 52.5% female patients seeking treatment at an outpatient clinic in a North India tertiary care center in the last five years.[8] In our study, gender characteristics were similar to previous studies, which showed that more women sought medical therapy (61.90%) than men (38.10%). This may be because women pay more attention to their appearance and go for check-ups early.

In our study, the most common predilection for vitiligo was in the face, followed by the acral, arms, trunk, legs, and neck. These results are consistent with previous studies, which showed that the most common predilection was in the face, followed by the acral, trunk, legs, neck, and arms.[9] Vitiligo most commonly occurs in areas exposed to sunlight and areas that tend to be hyperpigmented under normal conditions, such as the face, dorsum manus, areola mammae, axilla, umbilicus, and genitalia. On the extremities, vitiligo often results from the Köebnerization response.[7]

The diagnosis of vitiligo is made clinically and classified into localized, generalized, and universal vitiligo. Localized vitiligo is divided into focal, segmental, and mucosal. Generalized vitiligo is divided into acrofacial, vulgaris, and mixed.[7] Ezzedine *et al.* classified vitiligo into segmental, non-segmental (acrofacial, mucosal, generalized, universal, and mixed) vitiligo, and undetermined (focal and mucosal focal).[10] The study of Alikhan *et al.*[7] stated that generalized vitiligo is the most common type, while the most common subtype is vitiligo vulgaris. The study of Dégboé *et al.* also noted that vitiligo vulgaris was the most common type (52.4%), followed by localized vitiligo (36.2%), segmental (9.8%), and universal (1.6%).[11] In our study, the diagnosis of vitiligo was made clinically and divided into vitiligo vulgaris, segmental vitiligo, acral vitiligo, and focal vitiligo. Following previous studies, vitiligo vulgaris was the most common subtype in our study.

Phototherapy with NB-UVB has been recognized as the primary therapy for progressive and extensive vitiligo.[1,12] The study of Liu *et al.*[3] investigated that NB-UVB phototherapy can be given as early as possible in acute vitiligo lesions with limited area and provides high efficacy. Phototherapy works as an immunosuppressant and increases melanocyte differentiation and melanin production.[13] The Vitiligo Working Group Phototherapy recommends administering NB-UVB 2-3 times a week with an initial dose of 200 mJ/cm^2.[5] The dose is increased by 50 mJ/cm^2 to achieve a minimal erythema dose in depigmented lesions or 600 mJ/cm^2.[1,14] In our study, NB-UVB phototherapy was administered 2-3 times a week with an initial dose of 200 mJ/cm^2, which was increased by 50 mJ/cm^2 every three phototherapy sessions up to a maximum dose of 500 mJ/cm^2.

VASI measurements have a more accurate calculation in assessing the response to therapy than just looking at clinical photography.[12] This measurement is a reliable and responsive quantitative test for determining the degree of depigmentation related to disease severity and therapy evaluation.[15] Body areas are divided into hand areas, upper extremities, trunk, lower extremities, and feet. The face and neck are counted separately. One palm (1%) was used to calculate the extent of the vitiligo lesion. The degree of depigmentation was divided into 10, 25, 50, 75, 90, or 100%. The VASI assessment is then calculated using the following formula:[4]

$$\text{VASI} = \text{body surface area (palms)} \times \text{depigmentation}$$

In our study, the average percentage decrease in VASI was 18%, with the most significant reduction being 66.25% after 36 phototherapy sessions. After 48 phototherapy sessions, the average percentage decrease in VASI was 22%, with the most significant decline being 62.50%. The study of Sehrawat *et al.* showed that the mean reduction in VASI after 36 phototherapy sessions was 36.66%.[16] Another study by Farag et al. stated a significant mean decrease in VASI of 29.14% after 36 phototherapy sessions.[17] The results of those previous studies are higher than our study. This could be due to differences in predilection and disease duration not mentioned in those studies. Predilection and duration of the disease can influence response to therapy. Based on a systematic review study, the best response to phototherapy (repigmentation >75%) occurred in the face and neck (44.2%), followed by the trunk (26.1%), extremities (17.3%), hands (0%), and legs (0%).[18] In our study, the predilection of vitiligo patients who received phototherapy was highest on the face and acral (71.43% and 61.90%, respectively). The best response may also occur in vitiligo with disease duration <2 years before phototherapy.[19] The study of Liu et al.[3] stated a significant change in VASI after 60 phototherapy sessions, with a mean difference of 44.57%. The outcome of VASI reduction in that study was higher than our study, possibly because it only included vitiligo that had <3 months disease duration, localized lesions <5% BSA, and longer duration of phototherapy with a uniform frequency of three times a week.

The VASI is an analog of the psoriasis area and severity index (PASI). A 50% decrease in VASI (50) is analogous to a clinical improvement equivalent to PASI 75.[20] Based on the study of Sehrawat *et al.* and Kawakami and Hashimoto,[16,20] the decrease in VASI was divided into the following: a) VASI <10% (minimally improved), b) VASI 10-25% (improved), c) >25-50% (much improved), and d) VASI >50% (very much improved).

In our study, the most common responses after 36 and 48 phototherapy sessions were minimally improved (decrease in VASI<10%) and improved (reduction in VASI 10-25%). The mean decline in VASI was 18% and 22% after 36 and 48 phototherapy sessions, respectively. These results showed improvement in response to therapy. 9.52% and 6.67% of patients experienced a decrease in VASI >50% after 36 and 48 phototherapy sessions, respectively. These results indicate that there was very much improvement in these patients. Patients who experienced a decrease in VASI >50% after 48 sessions of phototherapy were fewer due to a reduction in the number of patients who followed phototherapy until the 48th session of the study period. A meta-analysis study showed that 50% of repigmentation occurred in 37.4% of patients after six months and in 56.8% of patients after 12 months of phototherapy. More repigmentation (75%) occurred in 19.2% of patients after six months and 35.7% after 12 months.[18] This pattern suggests a longer follow-up is needed to assess the VASI score reduction in more patients, especially in patients with a slow response.

Our study showed that 19.05% and 6.67% of patients did not experience a change in VASI after 36 and 48 phototherapy sessions, respectively. These patients had increased repigmentation of some lesions, although no VASI changes were found. This is because the addition of very little repigmentation has not reduced VASI. Treatment failure occurred if no repigmentation was found after 48 phototherapy sessions or up to 72 sessions in slow-response vitiligo.[5] In our study, all patients had repigmentation, although there were patients whose VASI did not change. Therefore, none of the patients were categorized as treatment failure.

A combination of topical therapy and phototherapy can be

given to patients with vitiligo.[1] In our study, there was little difference in VASI reduction between patients with vitiligo receiving combination therapy or monotherapy with UVB-NB phototherapy after 36 and 48 phototherapy sessions. This result differs from a systematic review study by Li *et al*. (2017),[21] which concluded that combining NB-UVB phototherapy with topical calcineurin inhibitors is superior to monotherapy with NB-UVB, especially in the face and neck area. This is probably due to the second most common location for patients with vitiligo in our study, the acral area (61.90%), which had a slower repigmentation and a small sample size. Furthermore, a meta-analytic study by Dong *et al.* (2021) found that the combination of NB-UVB phototherapy with 0.1% tacrolimus was better than phototherapy alone, especially in the face and proximal extremities.[22] In our study, the tacrolimus dose was 0.03%, lower than those studies, and the most predilection was in the acral region. Another modality for combination therapy with a topical corticosteroid. A study by Batchelor *et al.* (2020) reported that combining NB-UVB phototherapy with topical corticosteroids was superior to phototherapy alone.[23] Our result showed no difference in combination therapy with a topical corticosteroid. This may be due to the shorter duration of our study compared to that study, which has a more extended follow-up period of up to 9 months of therapy. Longer follow-up is required to assess the success of treatment.

Conclusions

Here, we report the characteristics and decreased VASI of patients with vitiligo treated with NB-UVB phototherapy. In our study, most cases were vitiligo vulgaris, with the most common predilection in the facial area following previous studies. A decrease in VASI occurred in most patients after 36 and 48 phototherapy sessions indicating improvement of the lesion. The results of our study are different from previous studies, which may be due to the predilection and duration of the disease. VASI assessment can be used to evaluate the response to phototherapy in patients with vitiligo. However, the weakness of VASI measurement as a tool for assessing response to therapy is that it cannot show a reduction in vitiligo patients with slight repigmentation in slow-response patients.

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