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Response of narrowband ultraviolet-B phototherapy combined with superoxide dismutase antioxidant cream in the management of non-segmental vitiligo

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ABSTRACT

Vitiligo is a skin depigmentation disorder characterized by the loss of melanocyte function. The oxidative stress theory plays a role in the occurrence of vitiligo. Narrow band ultraviolet B (NB-UVB) phototherapy can be combined with other therapies to accelerate skin repigmentation. A 47 yo woman presented to the dermatology and venereology outpatient clinic in Dr. Sardjito General Hospital, Yogyakarta with a chief complaint of white patches on her face, neck, chest, and hands that had persisted for 11 yr. The patient had previously received NB-UVB phototherapy and a calcineurin inhibitor cream, but the symptoms persisted. Significant repigmentation of the lesion area was achieved after NB-UVB phototherapy combined with superoxide dismutase (SOD) antioxidant cream. NB-UVB phototherapy plays a role in immunomodulation, biostimulation, and reducing oxidative stress. The SOD helps clear superoxide radicals, preventing damage to melanocytes. The combination of NB-UVB phototherapy and antioxidant cream can be considered a treatment option for vitiligo.

ABSTRAK

Vitiligo merupakan kelainan depigmentasi kulit yang ditandai dengan hilangnya fungsi melanosit. Teori stres oksidatif berperan dalam terjadinya vitiligo. Modalitas fototerapi *narrow band ultraviolet* B (NB-UVB) dapat dikombinasikan dengan terapi lain untuk mempercepat terjadinya repigmentasi kulit. Seorang wanita berusia 47 tahun datang ke poliklinik kulit dan kelamin RSUP Sardjito, Yogyakarta dengan keluhan utama bercak putih pada wajah, leher, dada, dan kedua tangan sejak 11 tahun lalu. Pasien telah mendapat terapi fototerapi NB-UVB kombinasi krim *calcineurin inhibitor* sebelumnya dan keluhan menetap. Setelah dilakukan fototerapi NB-UVB kombinasi dengan krim antioksidan *superoxide dismutase* (SOD), didapatkan repigmentasi yang signifikan pada area lesi. Fototerapi NB-UVB berperan dalam imunomodulator, biostimulasi dan mengurangi stress oksidatif. *Superoxide dismutase* membantu dalam memecah radikal superoksida sehingga tidak terjadi kerusakan pada melanosit. Kombinasi fototerapi NB-UVB dan krim antioksidan dapat menjadi pertimbangan sebagai tatalaksana vitiligo.

Keywords:
vitiligo treatment; narrow-band UVB; superoxide dismutase; calcineurin inhibitor; combination

INTRODUCTION

Vitiligo is a skin depigmentation disorder with multifactorial etiology. It can affect people of all ages and ethnicities, with most cases occurring before the age of 20 yr. The prevalence of vitiligo is estimated at 0.5-2% of the global population, including both adults and children.[1] According to the latest consensus from the European Dermatology Forum, vitiligo can be classified into segmental, nonsegmental, mixed, and unclassified types, with nonsegmental being the most common form.[2] Vitiligo has a significant psychosocial impact, especially when it affects the face or hands, often leading to

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issues with self-confidence.[3]

Vitiligo is characterized by loss of melanocyte function. The exact pathogenesis of the disease is still unknown, but several theories of the mechanism have been proposed, including the genetic, autoimmune, neural, auto-cytotoxic, and oxidative stress theories.[1,4] The oxidative stress theory suggests that an imbalance in the reduction-oxidation (redox) conditions in the skin leads to the excess production of reactive oxygen species (ROS). The accumulation of ROS has toxic effects on all cell components such as proteins, potentially damaging melanocytes and creating depigmented patches.[5]

The treatment of vitiligo is a challenge for dermatologists. The goals of treatment include stopping the progression of lesions, stabilizing the condition, and stimulating repigmentation. Current treatments include topical therapy, systemic therapy, phototherapy, and surgical methods.[2] Narrowband ultraviolet B (NB-UVB) phototherapy is recommended as a primary for vitiligo.[6] NB-UVB phototherapy can be combined with other therapies, including antioxidants.[2] Superoxide dismutase (SOD) is an antioxidant that binds ROS in skin tissue.[7] Several studies have indicated that SOD can be used as a safe and effective combination therapy for the treatment of vitiligo.[8,9] However, reports on the effectiveness of SOD cream combined with NB-UVB phototherapy in treating vitiligo patients in Yogyakarta are still lacking. This paper reports a case of nonsegmental vitiligo in a 47 yo woman who shows improvement with the combination of NB-UVB phototherapy and superoxide dismutase antioxidant cream. This case report aims to describe combination therapy that can be used as a treatment for vitiligo.

CASE

A 47 yo woman came to the dermatology and venereology outpatient clinic at Dr. Sardjito General Hospital, Yogyakarta with a chief complaint of milky white spots on her face, chest, and hands. The patient reported that the spots had first appeared on her neck 11 yr ago. The spots were neither itchy nor painful but had gradually spread to the face. She was diagnosed with vitiligo and initially treated with a combination of NB-UVB phototherapy and tacrolimus cream (Protopic®). The white spots began to decrease after one year of treatment. However, when tacrolimus cream became difficult to obtain, she was switched to pimecrolimus cream (Elidel®). After using pimecrolimus cream for one yr, the white spots persist and the patient complains of skin irritation, leading them to stop the treatment. Seven mo ago, she returned to the clinic due to the spread of white spots to her chest, face, and hands. The patient had no history of hyperthyroidism or other autoimmune diseases. She denied any drug allergies, and there was no family history of similar complaints. The patient is a housewife with two sons, and no other family members suffer from a similar disease.

On physical examination, the patient was compos mentis. Vital signs are within normal limits. Dermatological examination revealed multiple depigmented macules and patches with clear boundaries and irregular edges on the face, neck, chest, and hand. (FIGURE 1a). The vitiligo area scoring index (VASI), a standardized tool for assessing vitiligo extent and progression, was used to evaluate lesion severity (score range from 0-100). The VASI score is calculated by multiplying the percentage of vitiligo involvement in a body area by the extent of depigmentation within each patch. Initial VASI scores were: face (2.3), neck (0.3), chest (1.3), and hands (1.65). She was treated with NB-UVB phototherapy twice/wk with an initial dose of 200 mJ/cm^2 which was increased

by 50 mJ/cm^2 every three sessions, up to a maximum dose of 550 mJ/cm^2 per session. Additionally, she was prescribed superoxide dismutase antioxidant cream applied twice daily to the affected areas.

After 4 mo, there was noticeable repigmentation on the face, neck, and chest. However, in the 5th month, new depigmented lesions were found on the hand area, so the patient was then given oral methylprednisolone mini pulse therapy at a dose of 16 mg three times a week. After 60 phototherapy sessions (7 mo), significant improvement was observed, particularly in the face and neck areas, but only minimal improvement was seen on both hands (FIGURE 2b and c). The final VASI score was 1.04 for the face, 0.12 for the neck, 0.87 for the chest, and 1.61 for the hands (TABLE 1). In addition, no side effects were reported after using SOD antioxidant cream for 7 mo.

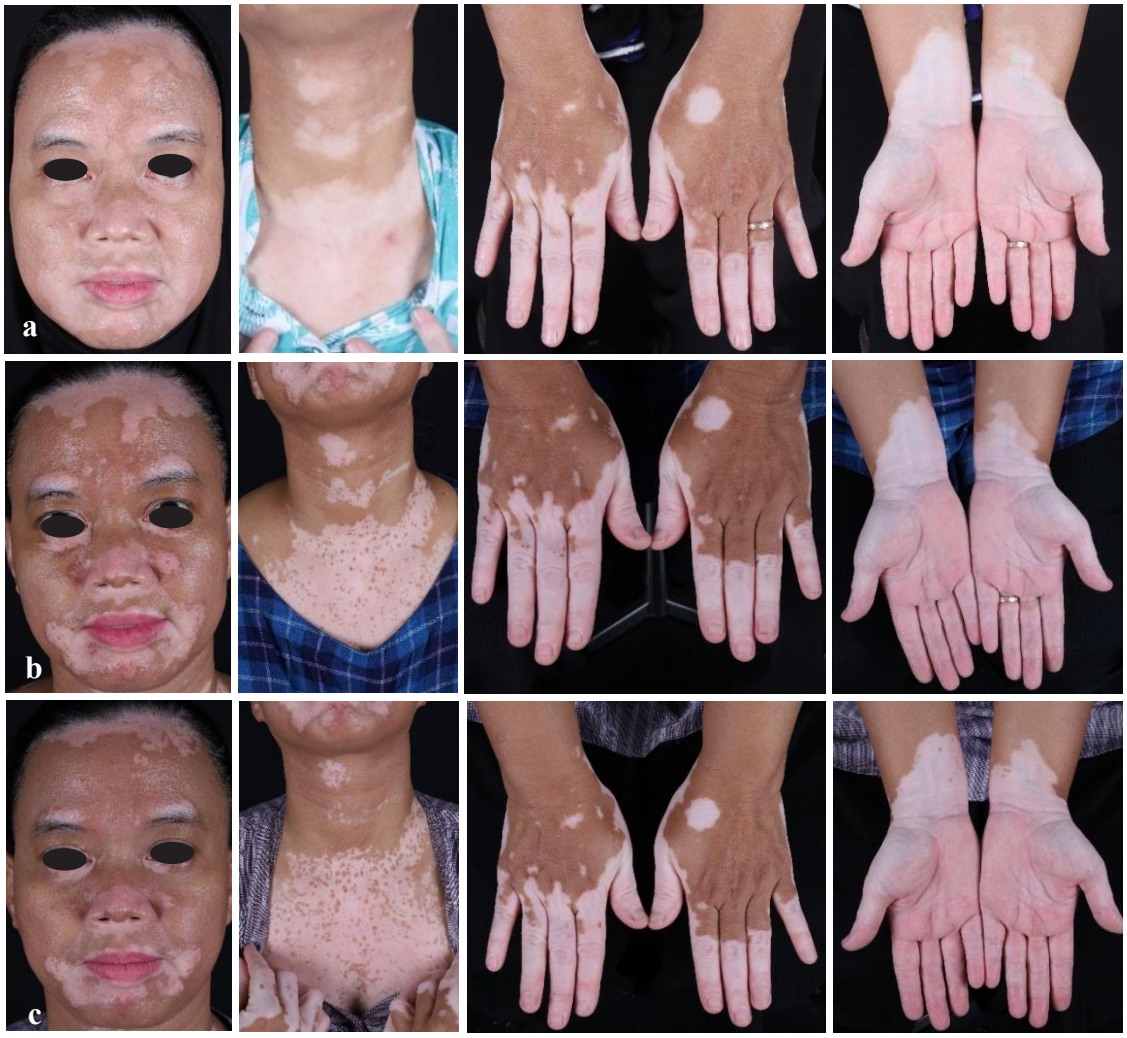

FIGURE 1. Clinical progression of vitiligo lesions a. Baseline presentation showing depigmented macules and patches with clear margins on face, neck, and hands; b. Partial repigmentation after 4 mo of combined NB-UVB phototherapy and superoxide dismutase antioxidant cream treatment; c. Further improvement after 7 mo of therapy, demonstrating marked repigmentation, particularly in facial and neck regions.

TABLE 1. VASI scores at baseline, after 4 and 7 mo in combination with NB-UVB phototherapy and superoxide dismutase antioxidant cream.

Area	VASI (vitiligo area severity index)			Decreased VASI (%)
	Baseline	4th month	7th month	
Face	2.3	2.05	1.04	52.7
Neck	0.3	0.24	0.12	60.0
Chest	1.3	1.22	0.87	33.0
Hands	1.65	1.64	1.61	0.02

DISCUSSION

The NB-UVB phototherapy has proven effective in treating vitiligo. It uses polychromatic light with a peak emission wavelength of 311 to 313 nm.[10] The Vitiligo Working Group has published recommendations for NB-UVB phototherapy, including dosing protocols (initial dose at 200 mJ/cm2, and increasing by 10-20% per session), frequency (optimally 3 times/wk), and maximum dose (1,500 mJ/cm2 for the face and 3,000 mJ/cm2 for the body) with a minimum of 48 exposures.[6] However, we believe that increasing the dose every 3 sessions is a viable approach. Our protocol of increasing the dose by 50 mJ/cm² every third session, rather than the standard 10-20% per treatment, was chosen to minimize the risk of phototoxicity while maintaining therapeutic effectiveness. This modified approach allowed for better monitoring of skin response between dose increases and allowed the skin more time to adapt to UV exposure, thereby reducing the risk of side effects such as erythema.[11]

The mechanism of NB-UVB phototherapy involves 2 stages. In the unstable vitiligo stage, it acts as an immunomodulator stimulating the expression of epidermal interleukin-10 (IL-10) which induces regulatory T lymphocytes to inhibit autoreactive T lymphocytes.[10] In the stable stage, it encourages the remaining follicular melanocytes to initiate repigmentation, known as the biostimulation effect, and helps stabilize the depigmentation process It is considered a relatively safe and effective treatment for vitiligo, yielding positive histological and clinical results with minimal adverse effects.[12] Additionally, NB-UVB reduces oxidative stress in vitiligo patients.[10]

Oxidative stress is a key factor in vitiligo pathogenesis. It disrupts redox homeostasis, leading to an imbalance between prooxidants and antioxidants. Oxidative stress can cause vitiligo through various mechanisms. The first mechanism involves interfering with the melanin synthesis process by inducing the release of high mobility group box 1 (HMGB1) protein, which downregulates proteins related to melanin biosynthesis.[7] Additionally, excessive accumulation of reactive oxygen species (ROS) can destabilize, synthesize, and disrupt lipid circulation in melanocytes. This leads to damage to the mitochondrial electron transport chain, further increasing ROS production and creating a vicious cycle that ultimately destroys melanocytes.[13] Moreover, oxidative stress is a significant factor in inducing the release of chemokines from keratinocytes which trigger the migration of CD8+ T cells into skin tissue, resulting in melanocyte death.[14]

Antioxidants are compounds that significantly reduce or prevent the harmful effects of free radicals on the

human body. They can be categorized based on their structure, solubility, and the kinetic processes they involve. Natural antioxidants are present in the skin because it is frequently exposed to various environmental factors.[7] Superoxide dismutase, a metalloenzyme, plays a crucial role in breaking down superoxide radicals (O_2^-) into H_2O_2 and O_2[15] This process helps reduce oxidative stress and inhibits the activation of inflammatory mediators, thereby preventing damage to melanocytes.[16] Topical SOD has shown good tolerability in clinical studies, with no reported side effects.[15] In contrast to calcineurin inhibitors as the primary topical therapy for vitiligo, most studies have identified burning, pruritus, erythema, skin atrophy, and facial flushing after alcohol consumption as the primary side effect.[11,17]

The combination management of NB-UVB phototherapy and SOD antioxidant cream in Indonesia is still rarely reported. Kostović *et al.*,[9] in 2007 reported that among 22 vitiligo patients, repigmentation was observed in approximately 57.9% of patients who received combination therapy of NB-UVB phototherapy and SOD antioxidant cream after 6 mo of treatment. The areas that showed significant repigmentation were the face and neck. The combination of NB-UVB and SOD cream is believed to provide a better therapeutic effect through the reduction of oxidative stress. NB-UVB reduces oxidative stress by balancing the oxidant-antioxidant system, while SOD directly neutralizes free radicals. However, different results were found in a study conducted by Yuksel *et al.*[18] in 2009, where repigmentation occurred in less than 50% of the total 30 subjects studied. The ratios in this study were lower than those reported by Kostović *et al.*,[9] even though the treatment protocol and duration were similar. This discrepancy may be attributed to differences in patient populations across geographical regions and variations in lesion evaluation methods.[18]

The variable treatment response observed in our patient warrants further analysis. While the face and neck areas showed notable improvement (52.7 and 60.0% VASI reduction, respectively), the hands demonstrated minimal change (0.02%). This pattern aligns with existing literature suggesting that acral areas like hands generally show more resistance to repigmentation. Several factors may contribute to this differential response. Acral areas naturally have a lower density of melanocytes compared to other skin regions. This results in a slower and less effective response to therapies, such as phototherapy.[19] The addition of oral mini-pulse steroid therapy was initiated specifically to address the hand lesions. Minipulse dose therapy with oral steroids is a good therapeutic option to arrest the activity of progressively unstable vitiligo.[20] While the combination of NB-UVB and topical SOD shows promise in vitiligo treatment, further large-scale, randomized controlled trials with standardized protocols and longer follow-up periods are needed to confirm its efficacy and optimize treatment strategies.

CONCLUSION

This case demonstrates the potential efficacy of combining NB-UVB phototherapy with superoxide dismutase antioxidant cream in treating non-segmental vitiligo. The synergistic effects of these modalities, targeting both oxidative stress and immune responses, resulted in significant improvement, particularly in the facial and neck areas. However, the variable response across different body sites, notably the unstable lesions on hands requiring additional systemic therapy, such as oral steroid minipulse dose, highlights the need for individualized treatment approaches.

Further controlled studies are warranted to establish optimal protocols for combination therapy, especially for resistant areas. The integration of antioxidant therapy in vitiligo management represents a promising strategy, particularly when combined with established treatments like NB-UVB phototherapy.

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