



NB-UVB Phototherapy Combined with Tacrolimus Ointment in Vitiligo Treatment

**Ayesha Siddiqua^{a*}, Md Mahabubur Rahaman^{bo},
Mohammad Rahmat Ullah Siddique^{c#}, Anzirun Nahar Asma^{d†}
and Sabrina Akter^{b‡}**

^a Delta Medical College and Hospital, Bangladesh.

^b Aurora skin and Aesthetics, Bangladesh.

^c Department of Dermatology, Banghabandhu Sheikh Mujib Medical University, Bangladesh.

^d Popular Medical College and Hospital, Bangladesh.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AS and SA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MMR, MRUS and ANA managed the analyses of the study. Authors MRUS and ANA managed the literature searches. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/92672>

Original Research Article

Received 20 August 2022

Accepted 27 October 2022

Published 31 October 2022

ABSTRACT

Background: Vitiligo, often referred to as a common and chronic disorder in which the skin loses its pigment or melanocyte-generating cells, causing hypopigmentation or depigmentation of affected area skin. Various treatment modalities such as topical, systemic and phototherapy are employed to treat this disease.

Objective: Vitiligo is often treated with phototherapy that utilizes narrowband ultraviolet B (NB–UVB). This study aims to investigate the effectiveness of combination therapy of NB–UVB phototherapy and tacrolimus in vitiligo treatment.

Methods: Minimal Erythema Dose (MED) was not calculated & an initial dose of 300 mj/cm² was started in all adult patients & 150 mj/cm² in children. Treatment was administered 2 times in a week on non-consecutive days. A retrospective questionnaire-based study was conducted for seven months (August 2019 to February 2020). About 95 patients with vitiligo in Dhaka were taken for

^o Senior Consultant;

[#] Research Assistant;

[†] Associate Professor;

[‡] Assistant Registrar;

*Corresponding author: E-mail: doctorserviceBRC@gmail.com, ayeshazamil17@gmail.com;

observation. Microsoft Office Excel 2010 software was used to do the analysis.

Results: In this study, 34.37% of patients were male, and on the other side, about 65.63% of patients were female. And most of the patients were young aged (21-30). In this case, females are mostly conscious of their skin health. One hundred forty lesions were treated on the face, extremities, and trunk. Excellent results were achieved in 66.43% (93/140) lesions, while 20.71% (29/140) lesions exhibited a good response. The response was termed poor as the extent of pigmentation achieved was less than 12.86% (18/140).

Conclusion: In this study, we found that the combination of NB-UVB phototherapy and tacrolimus is potentially effective in vitiligo, with the face and extremities (proximal part) responding better than other body sites.

Keywords: Vitiligo; narrowband ultraviolet b; tacrolimus; Dhaka; Bangladesh; etc.

ABBREVIATIONS

NB-UVB : *Narrow band Ultraviolet-B*

MED : *Minimal Erythema Dose*

1. INTRODUCTION

Vitiligo has emerged as a significant psychosocial issue in Bangladesh in recent years. Surprisingly, due to their lack of awareness about health, most people indicate that this ailment is a contagious sickness. Vitiligo, often referred to as "Sheti" in our region, is a pigmentary disorder of the skin and mucous membrane that results destruction of melanocytes leading to hypopigmentation or depigmentation of skin. It usually appear as a white spots on body. The lesions are characterized by well demarcated hypo pigmented or depigmented macules or patches, usually on face, trunk, hands, feet, lips; however, can occur any portion of the body [1]. On the basis of distribution it can be classified as Segmental & Non segmental (focal, acrofacial, mucosal, generalized). Approximately 1–2% of the world's population is affected by this depigmenting condition [2]. There have been a number of hypotheses put up on the causes of this condition; however, the most convincing evidence points to the interaction of environmental, genetic, and immune system variables as the primary contributor to autoimmune melanocyte loss [3]. Vitiligo is defined by the appearance of white patches on the skin that are circular in shape and develop in size over the course of time or, in very rare situations, heal on their own [4]. Vitiligo sufferers have access to a wide variety of therapies, each of which varies in the degree to which it is effective. The use of corticosteroids, immunomodulators, skin grafts, pseudocatalase, and phototherapy are some of the available

therapeutic options at this time [5]. Since narrow band ultraviolet B radiation (NB-UVB) has shown to be effective in treating vitiligo in clinical trials, it is now the treatment of choice for the condition [6]. On the other hand, high-dose administration poses a risk due to the phototoxicity of UVB, which may affect lesional as well as non-lesional skin [7].

Although the actual etiology is of vitiligo is unknown. Various theories about pathogenesis of this disorder and its etiology is multifactorial. It is oftenly related with genetic or non-genetic factors. Though numerous hypothesis have been proposed. These hypothesis are about destruction of melanocytes, which can be caused cytotoxic mechanisms, autoimmune mechanisms, intrinsic melanocyte defects, neural mechanisms, and oxidant-antioxidant mechanisms [8]. In neural hypothesis, the destruction of melanocytes are caused by neurochemical mediators [9].

The treatment of vitiligo is often and unsatisfactory and remains a challenge for the dermatologist, although numerous options have been proposed and are currently available [10]. A recent studies considered narrowband ultraviolet B (NB-UVB) as an effective and safe 1st line treatment of vitiligo [11-15]. Topical tacrolimus is also an additional option for the treatment of vitiligo that offers the advantages over corticosteroids [16-20]. Several studies have emphasized the possible usefulness and synergistic activity of the combination therapy of topical tacrolimus plus UVB phototherapy, with either NB-UVB or excimer laser [21-23].

The aim of this study was to evaluate the effectiveness and safety of the association of NB-UVB and topical tacrolimus for the treatment of vitiligo refractory to conventional therapies.



Fig. 1. Patient of vitiligo. Visual representation of effectiveness of NB-UVB, found from Aurora Skin and Aesthetics. Before treatment (i) & after treatment (ii)

2. MATERIAL AND METHODS

The current protocol is comprised of a short explanation of the research type, the length of the study, the study design, the inclusion and exclusion criteria, the operational mode of operation, and the fieldwork.

Study type: A retrospective questionnaire-based study.

Study duration: 7 months (August 2019 to February 2020)

Study design: Between the dates August 2019 and February 2020, a study was carried out in the city of Dhaka to determine the pattern of vitiligo as well as the treatment for it at the tertiary health care level. A study of 95 vitiligo patients who exhibited the signs and symptoms of the condition was carried out.

Inclusion and exclusion criteria: At the Aurora Skin and Hair Research Institute, all of the vitiligo

patients came for treatment, and while they were there, the patients were observed for research purposes. Patients who did not exhibit a sufficient number of signs and symptoms of vitiligo during the trial were not considered for inclusion.

Operational modality: The Microsoft Office Excel 2010 software was used to analyze the data about age, sex, biophysical features, diagnosis, therapy, possible medicines that cause vitiligo, the kind of vitiligo, and drugs used to control vitiligo symptoms.

Data collection form: The information that was requested on the data collecting form included the patient's identity number, as well as their name, gender, marital status, age, personal history, age distribution, and other relevant information. In addition, the causes of vitiligo, signs, and symptoms of the disease, side effects of various medications, different treatment options, numerous home remedies, and other alternative treatments were included in the questionnaires.

Research Framework: All field interviewers were well-versed in the theory behind data collection methods and the practical use of those methods, and both were experts in the disease they were studying. Patients were educated on the study's goals, and those who were comfortable doing so signed an informed consent form.

Patients were randomly assigned to either an intervention or a control group, with recorded demographic information such as age, sex, and disease duration. Patient's occupations, family histories, socioeconomic positions, dietary habits, and social problems were all documented in this socio-demographic study.

3. TREATMENT PROTOCOL

As all patients were skin types 3 & 4. Minimal Erythema Dose (MED) was not calculated & an initial dose of 300 mj/cm² was started in all adult patients & 150 mj/cm² in children. Treatment was administered 2 times in a week on non-consecutive days.

The irradiation dose was increased by 20% for each subsequent visit till the optimal amount was achieved to obtain minimal erythema in the lesions. During treatment, affected parts were only exposed & genitalia & other uninvolved areas were protected. Eyes were protected by the UV-blocking goggles. The maximum

treatment period was 6 months or earlier or if 75% or greater repigmentation was achieved.

4. RESULTS AND DISCUSSION

4.1 Age and Sex Distribution

In this study, 34.37% of patients were male, and on the other side, about 65.63% of patients were female. And most of the patients were young aged (21-30). In this case, females are mostly conscious of their skin health (Fig. 2).

4.2 Result

4.2.1 Age and sex distribution

In this study, 34.37% patients were male and on the other side about 65.63% patients were female. And most of the patients were from young aged (21-30). In this case, we can say female mostly conscious about their skin health.

4.3 Clinical Types of Vitiligo

In this research, we tried to classify the type of vitiligo in three sections as inactive, progressive and stable. The category of vitiligo was divided into generalized, acral & segmental. The number of the cases is included on the Table 1.

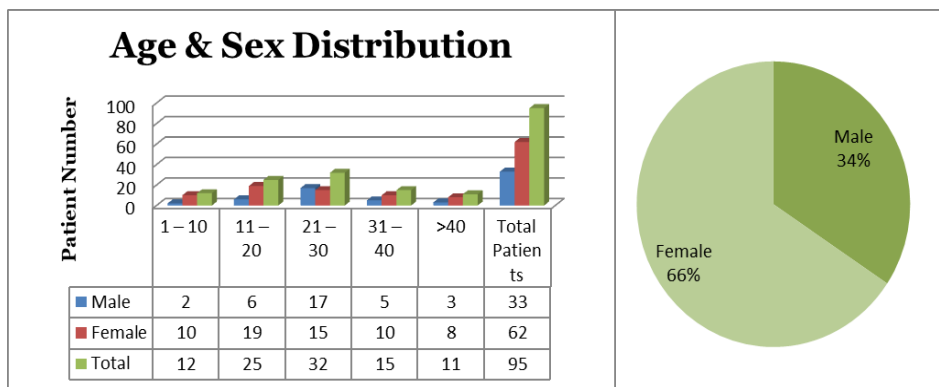


Fig. 2. Distribution of the participant by age and sex

Table 1. Clinical types of vitiligo among the patients

Type of Vitiligo	Inactive	Progressive	Stable	Total
Generalized	20	6	-	26
Acral	13	9	1	23
Focal	21	6	4	31
Segmental	7	3	5	15

Table 2. Result of the combination therapy of NB-UVB phototherapy and tacrolimus in vitiligo treatment.

Response	Face	Trunk	Extremities	Total
Excellent	38	22	33	93
Good	12	6	11	29
Poor	7	6	5	18

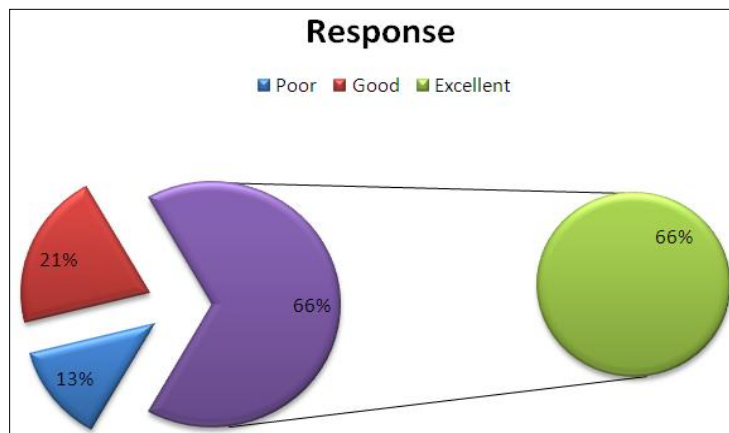


Fig. 3. A total response of the combination therapy of NB-UVB phototherapy and tacrolimus in vitiligo treatment

4.4 Response of Vitiligo

In this study, we tried to classify the treatment response in three sections as excellent, good and poor. The phototherapy was applied on the site of face, trunk and extremities. The number of the response is included on the Table 2.

140 lesions were treated on the face, extremities, and trunk. Excellent results were achieved in 66.43% (93/140) lesions, while 20.71% (29/140) lesions exhibited a good response. The response was termed as poor as the extent of pigmentation achieved was less than 12.86% (18/140) (Fig. 3).

5. DISCUSSION

Phototherapy is one of the few treatment options available in dermatology that can compete with its rich history, proven track record of success, and low-risk profile. Currently, the forms of phototherapy used most often include heliotherapy, NB-UVB, PUVA, and UVA1. Psoriasis is the condition that is treated with this medication the most often; nevertheless, it is also used for atopic dermatitis, vitiligo, cutaneous T-cell lymphoma, and cutaneous sclerosis, amongst other skin conditions [24]. A comprehensive patient evaluation needs to be

carried out before the suggestion of phototherapy. It is vital to evaluate whether or not the patient can come to the treatment facility at least twice each week, and it is essential to seek any potential contraindications. Patients may have difficulty attending the sessions, which is one of the most significant disadvantages of the technique.

This treatment is often used in conjunction with other therapies, such as topical or systemic drugs. It is necessary to keep up with the patient's frequent monitoring to detect and treat any potential harmful effects. Phototherapy is known to be beneficial, and as such, it needs to be explored whenever it's at all feasible [25]. Vitiligo is the most frequent kind of depigmented condition. It is characterized by a loss of pigmentation in the skin, hair, and mucosal surfaces [26,27]. Its frequency seems to be equal between men and women, and there is no variation in the incidence of occurrence according to either skin type or race [28]. The average age at which it first manifests itself is roughly 24 years old. It has been hypothesized that autoimmune melanocyte loss is caused by a mix of environmental [16], genetic, and immunological variables interacting with one another [29]. This is the theory supported by the strongest body of data [30].

Vitiligo is a skin condition that can be treated with various treatment modalities [31]. Still, one that is gaining in popularity is NB-UVB phototherapy. Many clinical investigations in vitiligo have established the effectiveness of phototherapy [32], particularly NB-UVB phototherapy [33]. In addition, there are a few topical therapeutic options that, when combined with this treatment technique, have been demonstrated to have a synergistic impact [34]. Studies conducted in clinical settings have shown that the effectiveness of targeted phototherapy, which may include NB-UVB phototherapy [35], varies depending on the location of the vitiligo lesions being treated. Clinical research has shown that the face and legs respond the best to targeted phototherapy, while acral lesions respond the least favorably [36].

In this study, we found that the combination therapy of NB-UVB phototherapy and tacrolimus is potentially effective in vitiligo, with the face and extremities responding better than other body sites.

6. CONCLUSION

The treatment of vitiligo has always been a difficult therapeutic task. It is generally agreed that phototherapy is one of the most successful forms of therapeutic treatment available today. For instance, NB-UVB therapy, the effectiveness of which has been proved in a variety of patient groups, has developed into a well-established therapeutic option. With a success rate of 63% against this kind of the illness, NB-UVB therapy is the treatment of choice, especially in patients who suffer from active and widespread vitiligo [37]. It has been shown in the past that NB-UVB is a very effective therapy for stable vitiligo when less than 5% of the body is afflicted by the condition. This treatment is very risk-free and may even be given to young patients without any concerns. A lot of research has been done to determine which therapy for vitiligo is the most effective. There is now no medication that can reverse the effects of vitiligo since there is no general agreement about the condition's pathophysiology. There is a pressing need for further vitiligo therapy research, including randomized controlled trials.

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

The research was not issued by BMDC committee. The study design was conducted by Aurora skin and Aesthetics.

ACKNOWLEDGEMENTS

The authors of the present study would like to thank "aurora skin and aesthetics" for its cooperation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Eleftheriadou V. Reliability and validity of the Vitiligo Signs of Activity Score. *Br J Dermatol.* 2020;183(5):801-802.
2. Islam, Tawhid. Vitiligo and the way to recovery. News Article, Dhaka, Bangladesh: The Daily Star; 2018.
3. Allam M, Riad H. Concise review of recent studies in vitiligo. *Qatar Med J.* 2013; 2013:1–19.
4. Le Poole IC, Das PK, van den Wijngaard RM, Bos JD, Westerhof W. Review of the etiopathomechanism of vitiligo: A convergence theory. *Exp Dermatol.* 1993; 2:145–153.
5. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet.* 2015;386: 74–84. DOI: 10.1016/S0140-6736(14)60763-7.
6. Ghafourian A, Ghafourian S, Sadeghifard N, Mohebi R, Shokoochini Y, Nezamoleslami S, Hamat RA. Vitiligo: Symptoms, pathogenesis and treatment. *Int J Immunopathol Pharmacol.* 2014;27: 485–489.
7. Homan MW Linthorst, Spuls PI, Nieuweboer-Krobotova L, de Korte J, Sprangers MA, Bos JD, Wolkerstorfer A, van der Veen JP. A randomized comparison of excimer laser versus narrow-band ultraviolet B phototherapy after punch grafting in stable vitiligo patients. *J Eur Acad Dermatol Venereol.* 2012;26:690–695.
8. Henning SW, Jaishankar D, Barse LW, Dellacecca ER, Lancki N, Webb K, Janusek L, Mathews HL, Price RN, Le Poole IC. The relationship between stress and vitiligo: Evaluating perceived stress and electronic medical record data. *PLoS One.* 2020;15(1):e0227909. [PMC free article] [PubMed]
9. Cohen BE, Manga P, Lin K, Elbuluk N. Vitiligo and Melanoma-Associated Vitiligo: Understanding Their Similarities and

- Differences. *Am J Clin Dermatol.* 2020 Oct;21(5):669-680.
10. Whitton ME, Ashcroft DM, Barrett CW, Gonzalez U. Interventions for vitiligo. *Cochrane Database Syst Rev.* 2006;25: CD003263
 11. Scherschun L, Kim JJ, Lim HW. Narrow-band ultraviolet-B is a useful and well-tolerated treatment for vitiligo. *J Am Acad Dermatol.* 2001;44:999-1003.
 12. Gambichler T, Breuckmann F, Boms S et al. Narrow-band UVB phototherapy in skin conditions beyond psoriasis. *J Am Acad Dermatol.* 2005;52:660-670.
 13. Kanwar AJ, Dogra S. Narrow-band UVB for the treatment of generalized vitiligo in children. *Clin Exp Dermatol.* 2005;30: 332-336.
 14. Parsad D, Kanwar AJ, Kumar B. Psoralen-ultraviolet A vs. narrow-band ultraviolet B phototherapy for the treatment of vitiligo. *J Eur Acad Dermatol Venereol.* 2006;20: 175-177.
 15. El Mofty M, Mostafa W, Esmat S et al. Narrow-band Ultraviolet B 311 nm in the treatment of vitiligo: two right-left comparison studies. *Photodermatol Photoimmunol Photomed.* 2006;22:6-11.
 16. Grimes PE, Soriano T, Dytoc MT. Topical tacrolimus for repigmentation of vitiligo. *J Am Acad Dermatol* 2002;47:789-791.
 17. Tanghetti EA. Tacrolimus ointment 0.1% produces repigmentation in patients with vitiligo: results of a prospective patient series. *Cutis.* 2003;71:158-162.
 18. Lepe V, Moncada B, Castanedo-Cazares JP et al. A double-blind randomized trial of 0.1% tacrolimus vs. 0.05% clobetasol for the treatment of childhood vitiligo. *Arch Dermatol.* 2003;139:581-585.
 19. Silverberg NB, Lin P, Travis L et al. Tacrolimus ointment promotes repigmentation of vitiligo in children: a review of 57 cases. *J Am Acad Dermatol.* 2004;51:760-766.
 20. Kostovic K, Pasic A. New treatment modalities for vitiligo: focus on topical immunomodulators. *Drugs.* 2005;65: 447- 459.
 21. Castanedo-Cazares JP, Lepe V, Moncada B. Repigmentation of chronic vitiligo lesions by following tacrolimus plus ultraviolet-B-narrow-band. *Photodermatol Photoimmunol Photomed.* 2003;19:35-36.
 22. Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. *Dermatol Surg.* 2004;30: 130-135.
 23. Passeron T, Ostovari N, Zakaria W et al. Topical tacrolimus and the 308-nm excimer laser: a synergistic combination for the treatment of vitiligo. *Arch Dermatol.* 2004;140:1065-1069.
 24. Ujihara J.E., Ferreira F.R., Mandelbaum S.H. Phototherapy: experience from a reference service. *An Bras Dermatol.* 2017;92:745-746.
 25. Barros NM, Sbroglio LL, Buffara MO, Baka JLCES, Pessoa AS, Azulay-Abulafia L. Phototherapy. *An Bras Dermatol.* 2021;96 (4):397-407.
 26. Birlea SA, Spritz RA. Norris DA. Fitzpatrick's Dermatology in General Medicine. Edited by 8th. New York, USA: McGraw-Hill; 2014.
 27. Kyriakis KP, Palamaras I, Tsele E, Michailides C, Terzoudi S. Case detection rates of vitiligo by gender and age. *Int J Dermatol.* 2009;328 -329.
 28. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their relatives. *Pigment Cell Res.,* 2003:208 - 214.
 29. Ali khan A, Felsten LM, Daly M, Petronic-Rosic V. "Vitiligo: A comprehensive overview Part 1. *J Am Acad Dermatol.* 2011:473-491.
 30. Hann S-K, Nordlund J. Vitiligo."Oxford: Blackwell Science; 2000.
 31. Akar A, Tunca M, Koc E, Kurumlu Z. Broadband targeted UVB phototherapy for localized vitiligo: A retrospective study. *Photodermatol Photoimmunol Photomed.* 2009:161-163.
 32. Park KK, Liao W, Murase JE. A review of monochromatic excimer light in vitiligo." *Br J Dermatol.* 2012:468-478.
 33. Asawanonda P, Kijluakiat J, Korkij W, Sindhupak W. Targeted broadband ultraviolet B phototherapy produces similar responses to targeted narrowband ultraviolet B phototherapy for vitiligo: A randomized, double-blind study. *Acta Derm Venereol.* 2008:376-381.
 34. Asawanonda P, Charoenlap M, Korkij W. Treatment of localized vitiligo with targeted broadband UVB phototherapy: A pilot study. *Photodermatol Photoimmunol Photomed.* 2006: 133-136.
 35. Le Duff F, Fontas E, Giacchero D, Sillard L, Lacour JP, Ortonne JP. 308-nm excimer lamp vs 308-nm excimer laser for treating

- vitiligo: A randomized study. Br J Dermatol. 2012:188-192.
36. Passeron T, Ostovari N, Zakaria W, Fontas E, Larrouy JC, Lacour JP. Topical tacrolimus and the 308-nm excimer laser: A synergistic combination for the treatment of vitiligo. Arch Dermatol. 2004:1065-1069.
37. Njoo MD, Westerhof W, Bos JD, Bossuyt PM. The development of guidelines for the treatment of vitiligo. Clinical Epidemiology Unit of the Istituto Dermopatico dell'Immacolata-Istituto di Recovero e Cura a Carattere Scientifico (IDI-IRCCS) and the Archives of Dermatology. Arch Dermatol. 1999;135:1514–1521.

© 2022 Siddiqua et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://www.sdiarticle5.com/review-history/92672>