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RESEARCH ARTICLE

A STUDY TO COMPARE THE EFFICACY OF NARROWBAND-UVB ALONE VERSUS NARROWBAND-UVB WITH TOPICAL TACROLIMUS 0.1% IN TREATMENT OF VITILIGO.

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Abstract

Background: Vitiligo is a chronic skin condition characterized by the loss of pigment-producing cells, resulting in white patches on the skin. It affects 0.1-2% of people worldwide, regardless of gender or race, and can be particularly distressing for those with darker skin tones. While various treatment options have been studied, there is limited research comparing the effectiveness of narrow-band ultraviolet B (NB-UVB) therapy alone versus its combination with tacrolimus. This study aims to address this gap.

Aim: The aim of this study is to compare the efficacy of Narrowband-UVB therapy alone versus Narrowband-UVB therapy combined with topical tacrolimus 0.1% in treating vitiligo.

Methods: This was a randomized, open-label, prospective, comparative study, conducted over 18 months at the dermatology outpatient department of Basaweshwara Teaching and General Hospital, affiliated to Mahadevappa Rampure Medical College, Kalaburagi. 100 patients were enrolled, and demographic data were recorded during the initial visit. A comprehensive clinical and dermatological assessment was performed, including evaluation of the percentage of body surface area affected by vitiligo. 50 patients in Group 1 received Narrowband-UVB thrice weekly, while 50 patients in Group 2 received once-daily topical tacrolimus 0.1% in addition to Narrowband-UVB thrice weekly. The primary efficacy measure, Vitiligo Area Scoring Index (VASI), was assessed at baseline and every 2 months during the one-year follow-up period. Secondary efficacy was evaluated using Physician Global Assessment scores at the end of one year.

Results: The study found that combination therapy with Narrowband-UVB and tacrolimus 0.1% resulted in earlier and more substantial treatment responses compared to Narrowband-UVB alone after 12 months. There was a statistically significant reduction in vitiligo area as measured by VASI (P=0.001) with combination therapy, particularly noticeable on the face and trunk. Physician Global Assessment scores indicated minimal improvement in VASI reduction for 40% of patients in the Narrowband-UVB group compared to 16% in the combination therapy group. Definite improvement was observed in 48% versus 52% of patients, and marked improvement in 8% versus 24%, respectively. Excellent improvement was noted in 4% of patients in the Narrowband-UVB group compared to 8% in the combination therapy group.

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Conclusion: Combination therapy using Narrowband-UVB with tacrolimus 0.1% appears to be more effective than Narrowband-UVB alone for treating vitiligo. It resulted in earlier and more significant repigmentation, particularly on the face and trunk, with minimal side effects observed for both treatments. These findings suggest that combining Narrowband-UVB with tacrolimus could offer an enhanced therapeutic option for patients with vitiligo.

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Introduction:-

Vitiligo is a prevalent pigmentary skin disorder affecting approximately 1% of the global population. It is often accompanied by widespread prejudices, ignorance, taboos, and confusion with leprosy, leading to social embarrassment for affected individuals, even though it has no impact on life expectancy. [1]

Vitiligo is an idiopathic acquired depigmenting condition marked by depigmented macules of different sizes and the histological loss of functioning melanocytes from the epidermis. The most prevalent pigmentary condition involves a complicated interaction between hereditary and environmental variables that ultimately results in the loss of melanocytes, which leaves lesions that lack pigmentation. [2]

Varied populations have varied prevalence rates; among Caucasians (0.38%), Africans (0.34%), and Chinese (0.0093%), it is less common than among Indians (0.46–1.13%). India has recorded the highest incidence, followed by Mexico and Japan. Many explanations have been put forth, including those involving a genetic predisposition, neural and growth factor dysregulation, autoimmune phenomena, auto cytotoxicity, and innate cellular metabolic abnormalities that result in melanocyte apoptosis. [3]

Vitiligo manifests with diverse phenotypical expressions and various types of the condition are differentiated based on clinical presentation. The natural progression of the disease is gradual, unpredictable, and challenging to manage. At times, the disease remains stable for extended periods. A variety of medical and surgical treatments are available for vitiligo, encompassing options such as topical corticosteroids, immunomodulators, vitamin D3 analogs as well as modalities like PUVA and NBUVB phototherapy and interventions like cultured melanocyte suspensions, camouflage methods, skin grafting and psychological therapy. [4]

Despite numerous therapeutic options, the management of vitiligo remains unsatisfactory. Topical immunomodulators like tacrolimus and pimecrolimus do not induce skin atrophy, that is commonly associated with prolonged use of topical corticosteroids. Tacrolimus works by inhibiting T cell activation and by the blockade of calcineurin action and transcription of interleukins IL2, IL4, and IL5. In vitro studies have illustrated the beneficial effects of tacrolimus in vitiligo, revealing increased proliferation of melanocytes and melanoblasts in epidermal cell cultures. [5]

NBUVB is widely utilized in treating vitiligo. It functions by inhibiting the production and release of cytokines and by stimulating dormant melanocytes in the outer root sheath of hair follicles to proliferate and migrate into vitiligo lesions. There are limited studies comparing the effectiveness and tolerance of NBUVB therapy versus tacrolimus for treating vitiligo. More research is needed in this area to better understand their comparative efficacy. Therefore, this prospective study aims to introduce a relatively new treatment approach that may offer benefits to vitiligo patients. This treatment method could may provide rapid symptomatic improvement, thereby reducing the psychological distress associated with the cosmetic disfigurement caused by vitiligo.

Material and Methods:-

This was a randomized, open-label, prospective, comparative study conducted over 18 months at the dermatology out patient department of Basaweshwara Teaching and General Hospital, affiliated to Mahadevappa Rampure Medical College, Kalaburagi.The period of study was conducted from 1st August 2022 to 31stJanuary 2024.

100 patients were enrolled, and demographic data were recorded during the initial visit. A comprehensive clinical and dermatological assessment was performed, including evaluation of the percentage of body surface area affected by vitiligo. 50 patients in Group 1 received Narrowband-UVB thrice weekly, while 50 patients in Group 2 received once-daily topical tacrolimus 0.1% in addition to Narrowband-UVB thrice weekly. The primary efficacy measure, Vitiligo Area Scoring Index (VASI), was assessed at baseline and every 2 months during the one-year follow-up period. Secondary efficacy was evaluated using Physician Global Assessment scores at the end of one year.

Inclusion criteria

1. All diagnosed cases of Vitiligo in the age group 15-60 years
2. Patients with body surface area involvement less than 20%.

Exclusion criteria

1. Mucosal vitiligo
2. History of any treatment of vitiligo in preceding 3 months
3. History of photosensitivity or administration of drugs causing photosensitivity.
4. Pregnancy and lactation
5. Severe hepatic, renal and systemic skin disease.
6. If patient develops severe side effects/intolerant during treatment.

Assessment of treatment efficacy is done by

1. VASI (Vitiligo Area Scoring Index)
2. Physician global assessment

Standardized assessment for estimating the degree of pigmentation to calculate the Vitiligo Area Scoring Index (VASI) is as follows:

1. At 100% depigmentation, no pigment is present
2. At 90%, specks of pigmentation are present
3. At 75%, the depigmented area exceeds the pigmented area.
4. At 50%, the depigmented area and the pigmented area are equal
5. At 25%, the pigmented area exceeds the depigmented area.
6. At 10%, only specks of depigmentation are present.

VASI for each body region is calculated by the product of the area of vitiligo in hand units (which was set at 1% per unit) and extent of depigmentation with in each measured hand unit patch.
Total body VASI was then estimated by
Total BodyVASI=∑[handunits] X [residual depigmentation]

Percentage reduction in VASI in each body region of all patients were evaluated every two months till 1 year in patients of both the groups. The difference reduction of VASI initial (0 month) with last follow up VASI (12 months) were determined. The difference of test groups A & B was analysed using students "t"test. The VASI initial with all respective followups of each group were analysed separately. The mean difference reduction was obtained using paired t test. Using ANOVA (analysis of variance), the difference in reduction between VASI initial and final with respect to lesion area were analysed. The statistical analysis was obtained with the assumption of α = level of significance =95% confidence level. So, $p < 0.05$ is the cut-off value for statistical significance.

Physician global assessment

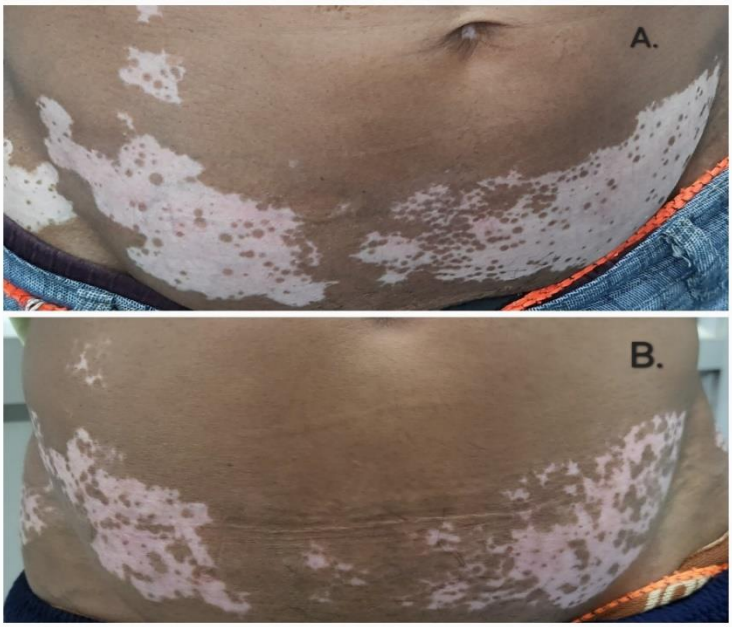
The scale is based on the degree of repigmentation within lesions over time.
The evaluation subjective is largely dependent on the human eye and judgment to produce the scorings.
Score improvement in percentage

1. 0% - No Change
2. 1-25% - Minimal improvement
3. 26-50% - Definite improvement
4. 51-75% - Marked improvement
5. 76-100% - Excellent improvement

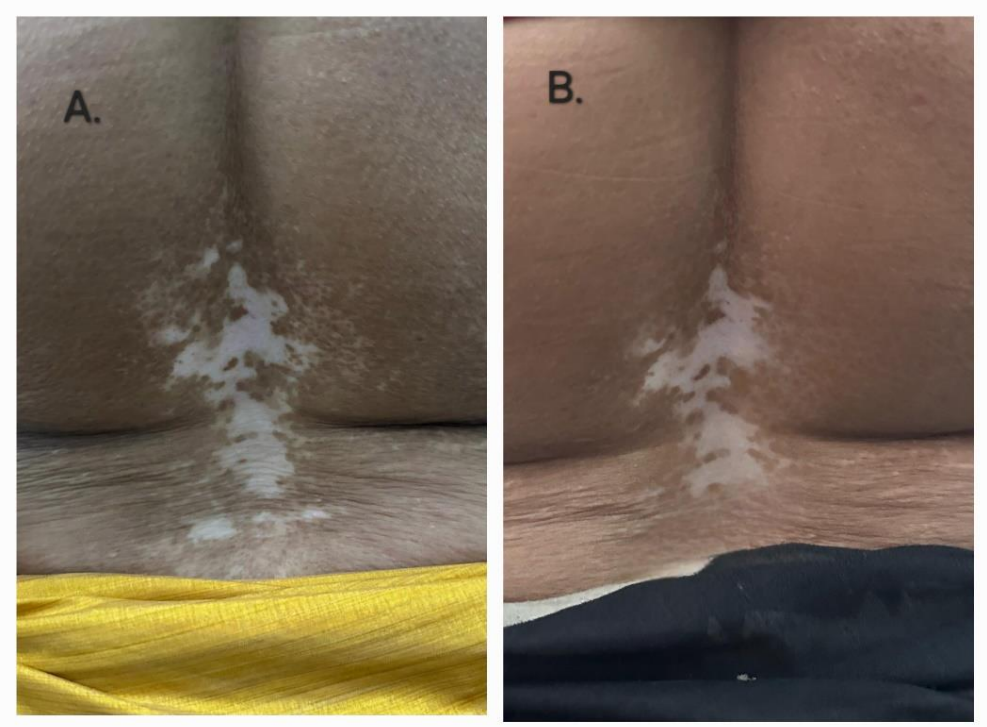
Results:-

Out of 110 patients enrolled in the study, only 100 patients completed the study. Six patients in Group 1(NBUVB) and four patients from Group 2 (NBUVB with 0.1% tacrolimus) group discontinued from study, so they were excluded from analysis. In this prospective study comparing two types of vitiligo treatment, NB-UVB was given to 50 patients having lesions in 64 areas totally and NB-UVB with topical 0.1 % tacrolimus was given to 50 patients having lesions in 68 areas in total. In both the groups, some patients have vitiligo lesions in more than one area. Hence total number of lesions vary in two groups. Age distribution in both the groups was in the range of 15-60 years. There is no significance difference between the age distributions in both the groups (p=0.93). The sex ratio between the groups was comparable but not statistically significant. The mean duration of disease in NB-UVB alone group was 17.76 months and NB-UVB with tacrolimus group was 17.52 months. 4 patients had associated disease in NB-UVB treated group, while none of the patients had associated disease in NB-UVB with tacrolimus group. The percentage distribution of lesion area was maximum in trunk, lower limb and upper limb in both the groups. In NBUVB group maximum number of patients had vitiligo involving 6-10% of total body surface area. In NBUVB with 0.1% tacrolimus group maximum number of patients had vitiligo involving 1-10 % of total body surface area. In Patients treated only with NB-UVB alone, only after 4 months follow up, mean VASI started reducing in face, lowerlimb, trunk and upper limb, but feet and hand areas not shown reduction in VASI. Mean VASI started to reduce at 6months of treatment in hand lesions and at 8 months in feet lesions. In patients treated with combination therapy, there was reduction of mean VASI score from 2 month follow up on the face, lower limb, trunk and upper limb but feet and hand areas show reduction in mean VASI only from 4 months follow up. On observing results of both the treatment modalities, NB-UVB with tacrolimus shows reduction in mean VASI earlier than NB-UVB alone during follow up. Lesions in feet and hand needs longer duration of treatment than in other areas in both modalities of treatment but NB-UVB with tacrolimus shows earlier response than NB-UVB alone in these areas. Mild side effects like itching, burning were minimal in both the groups. Out of 50 patients treated with NB-UVB, 8 patients had side effects. Similarly, in 50 patients treated with NB-UVB and tacrolimus ,4 patients had side effects due to treatment. Physician Global Assessment scores indicated minimal improvement in VASI reduction for 40% of patients in the Narrowband-UVB group compared to 16% in the combination therapy group. Definite improvement was observed in 48% versus 52% of patients, and marked improvement in 8% versus 24% and Excellent improvement was noted in 4% of patients in the Narrowband-UVB group compared to 8% in the combination therapy group.

Treatment with NB-UVB alone

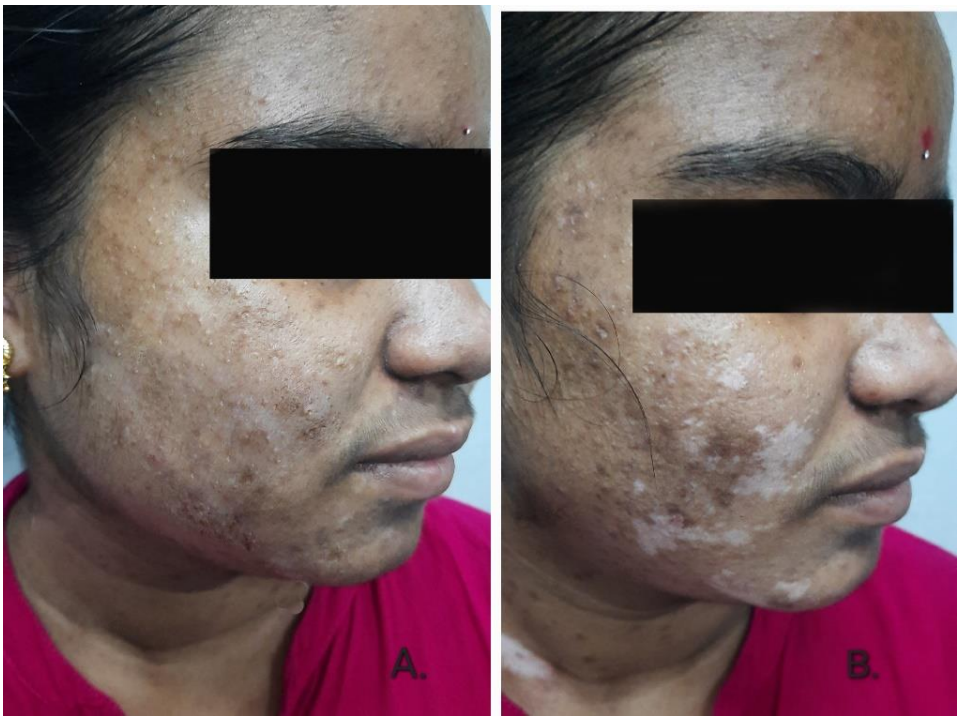


A.) Before treatment
B.) After 1 year of Treatment of NB-UVB alone

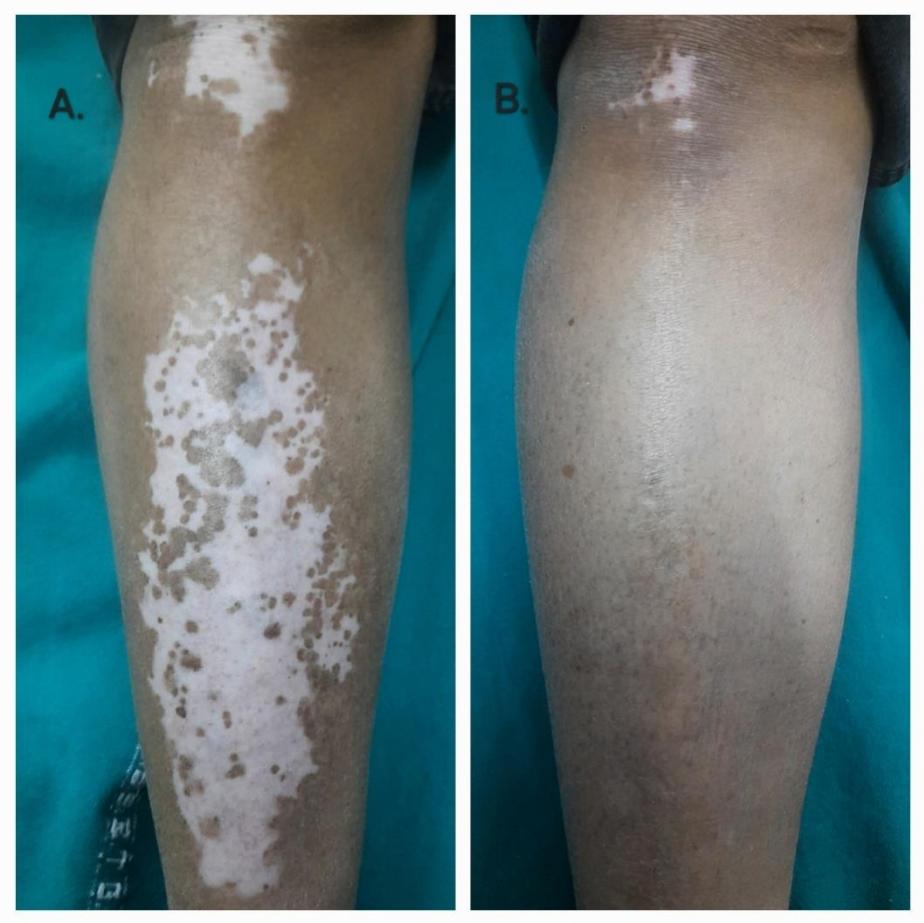


A. Before Treatment
B. After 1 year of Treatment of NB-UVB alone.

Treatment with Combination of NB-UVB and Topical Tacrolimus 0.1%



A. After 6 months of Treatment with combination of NB-UVB and Tacrolimus 0.1%.
B. Before treatment



A.) Before treatment.
B.) After 8 months of Treatment with combination of NB-UVB and Tacrolimus 0.1%.

Discussion: -

Vitiligo is a chronic skin condition characterized by the loss of pigment-producing cells, resulting in white patches on the skin. It affects 0.1-2% of people worldwide, regardless of gender or race, and can be particularly distressing for those with darker skin tones. While various treatment options have been studied, there's limited research comparing the effectiveness of narrow-band ultraviolet B (NB-UVB) therapy alone versus its combination with tacrolimus. The research compared two groups: one receiving only NB-UVB treatment and another receiving NB-UVB with tacrolimus. Both groups had similar baseline characteristics, including average disease duration of about 17.5 months. The sex ratio between the groups was comparable but not statistically significant. Results showed that the combination of NB-UVB and tacrolimus led to a statistically significant reduction in the Vitiligo Area Scoring Index (VASI). This finding aligns with previous studies, such as one conducted by Hs Satyanarayan et al[6]. in Chandigarh, which found slightly better repigmentation with the combination therapy, although their results weren't statistically significant. A study by Nordal et al[7] also concluded that adding tacrolimus ointment (0.1%) to NB-UVB treatment was more effective than NB-UVB alone, consistent with our results. Our study observed earlier treatment response and greater overall efficacy after 12 months in the combination therapy group. The reduction in vitiligo area, as measured by VASI, was statistically significant with the combination therapy. This aligns with findings from Majid et al., who reported that adding topical tacrolimus enhanced the repigmentation achieved with NB-UVB therapy.[8]Fai et al.'s study on the efficacy of combined NB-UVB and tacrolimus treatment showed repigmentation in over 70% of lesions, with better outcomes on the face, trunk, and limbs compared to extremities and genital areas. Our study similarly found that lesions on the face, trunk, and limbs responded better and earlier to the combination therapy, while hands and feet required longer treatment.[9]

A comparative study by Mehrabi D et al[10] showed better repigmentation with the combination therapy, although their results weren't statistically significant. In contrast, our study found statistically significant improvements in VASI reduction with the combination therapy. In a nutshell, NB-UVB with tacrolimus appears superior to NB-UVB alone for vitiligo treatment. It shows earlier and more significant repigmentation, especially on the face, trunk. Both treatments had minimal side effects, mainly transient erythema, burning, and itching. These findings suggest that combining NB-UVB with tacrolimus could offer an improved treatment option for vitiligo patients, although longer treatment may be necessary for hands and feet.

Conclusion: -

Narrow band-UVB with tacrolimus treatment is superior to Narrow band-UVB alone for treatment of vitiligo in terms of reduction in vitiligo area. Narrow band-UVB with tacrolimus shows earlier repigmentation than narrow band UVB alone in vitiligo (P= 0.001). Lesions in the face, trunk shows earlier re-pigmentation in patients treated with NB-UVB and tacrolimus. Lesions in hands and feet needs longer duration of treatment while comparing trunk, face, upper and lower limbs in both modalities of treatment. No severe side effects were noted. This treatment method provides safe and rapid symptomatic improvement, thereby reducing the psychological distress associated with the cosmetic disfigurement caused by vitiligo.

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