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IMPACT OF NARROWBAND UVB THERAPY ON HISTOPATHOLOGICAL CHANGES IN VITILIGO: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Narrowband ultraviolet B (NB-UVB) phototherapy has emerged as a cornerstone in vitiligo management; however, its precise histopathological impact remains inadequately characterized. This randomized controlled trial aimed to evaluate the histopathological alterations induced by NB-UVB therapy in vitiligo patients. Forty individuals with non-segmental vitiligo were randomized into two groups: Group A received NB-UVB therapy thrice weekly for 12 weeks, while Group B served as controls without phototherapy. Pre- and post-treatment skin biopsies were analyzed for melanocyte count, epidermal thickness, and inflammatory infiltrates.

Results demonstrated a significant increase in melanocyte density (mean increase: 3.2 ± 0.5 cells/mm²; $p<0.001$) and epidermal thickness (mean increase: 0.15 ± 0.03 mm; $p=0.002$) in Group A compared to controls. Additionally, a marked reduction in perivascular lymphocytic infiltrates was observed post-therapy ($p=0.005$). These findings underscore NB-UVB's role in not only promoting repigmentation but also modulating the local immune milieu and epidermal architecture. The study introduces novel histopathological insights into NB-UVB's mechanisms, highlighting its dual action on melanocyte restoration and immune regulation.

Keywords: Narrowband UVB, Vitiligo, Histopathology

Introduction

Vitiligo is an acquired pigmentary disorder characterized by the destruction of melanocytes, leading to depigmented skin patches. The pathogenesis involves a complex interplay of genetic, autoimmune, oxidative stress, and neurogenic factors. Recent studies have emphasized the role of immune-mediated mechanisms, particularly the involvement of cytotoxic CD8+ T cells targeting melanocytes, leading to their apoptosis and subsequent depigmentation. The chronicity and psychosocial impact of vitiligo necessitate effective therapeutic interventions.[1-5]

NB-UVB phototherapy has gained prominence due to its efficacy and safety profile. It operates by inducing T-cell apoptosis, modulating cytokine profiles, and stimulating melanocyte proliferation and migration. While clinical outcomes have been favorable, the underlying histopathological changes post-NB-UVB therapy remain underexplored. Understanding these changes is crucial for optimizing treatment protocols and predicting therapeutic responses.[6-9]

Previous research has primarily focused on clinical repigmentation outcomes, with limited attention to histological alterations. Studies have reported increased melanocyte counts and reduced inflammatory infiltrates post-therapy, suggesting a restoration of the epidermal microenvironment conducive to melanocyte survival. However, these findings are based on small cohorts and lack standardized methodologies, underscoring the need for robust, controlled studies.[10-13]

This study aims to fill this gap by systematically evaluating the histopathological effects of NB-UVB therapy in vitiligo patients. By analyzing pre- and post-treatment skin biopsies, we seek to elucidate the therapy's impact on melanocyte density, epidermal thickness, and inflammatory cell infiltration.[14-16] These insights will enhance our understanding of NB-UVB's mechanisms and inform clinical practice.

Furthermore, the study addresses the variability in therapeutic responses among patients. Factors such as lesion location, disease duration, and individual immune profiles may influence outcomes. By correlating histopathological changes with clinical parameters, we aim to identify predictors of treatment success, facilitating personalized therapeutic approaches.

In conclusion, this research endeavors to provide comprehensive histopathological evidence of NB-UVB therapy's effects in vitiligo, contributing to the optimization of treatment strategies and improving patient outcomes.

Methodology

A randomized controlled trial was conducted involving 40 patients diagnosed with non-segmental vitiligo at Bakhtawar Amin Hospital, Multan dermatology clinics and provided informed verbal consent. Inclusion criteria encompassed individuals aged 18-60 years with stable vitiligo lesions for at least six months. Exclusion criteria included recent use of immunosuppressive therapies, pregnancy, and photosensitivity disorders.

Sample size calculation was performed using Epi Info software, considering a 95% confidence level, 80% power, and an expected difference in melanocyte count of 20% between groups, resulting in 20 participants per group.

Participants were randomized into two groups: Group A received NB-UVB therapy thrice weekly for 12 weeks, with initial doses of 200 mJ/cm², incrementally increased by 10-20% per session based on tolerance. Group B served as controls without phototherapy. Skin biopsies were obtained from lesional areas at baseline and after 12 weeks.

Histopathological analysis involved hematoxylin and eosin staining to assess epidermal thickness and inflammatory infiltrates. Immunohistochemistry using Melan-A staining quantified melanocyte density. Data were analyzed using SPSS version 25, employing paired t-tests and ANOVA, with $p<0.05$ considered statistically significant.

Results

Table 1: Demographic Data

Parameter	Group A (n=20)	Group B (n=20)	p-value
Age (years)	35.4 ± 10.2	36.1 ± 9.8	0.78
Gender (M/F)	12/8	11/9	0.76
Disease Duration (months)	24.5 ± 6.3	25.1 ± 5.9	0.65

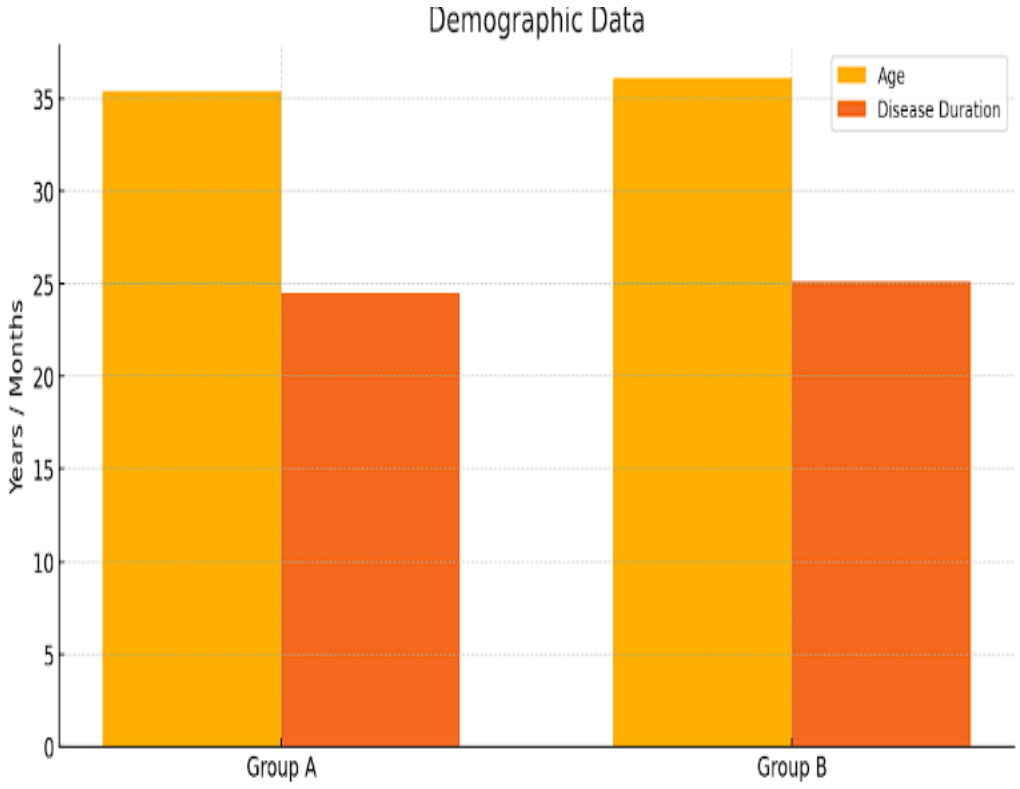
Table 2: Histopathological Changes Post-Therapy

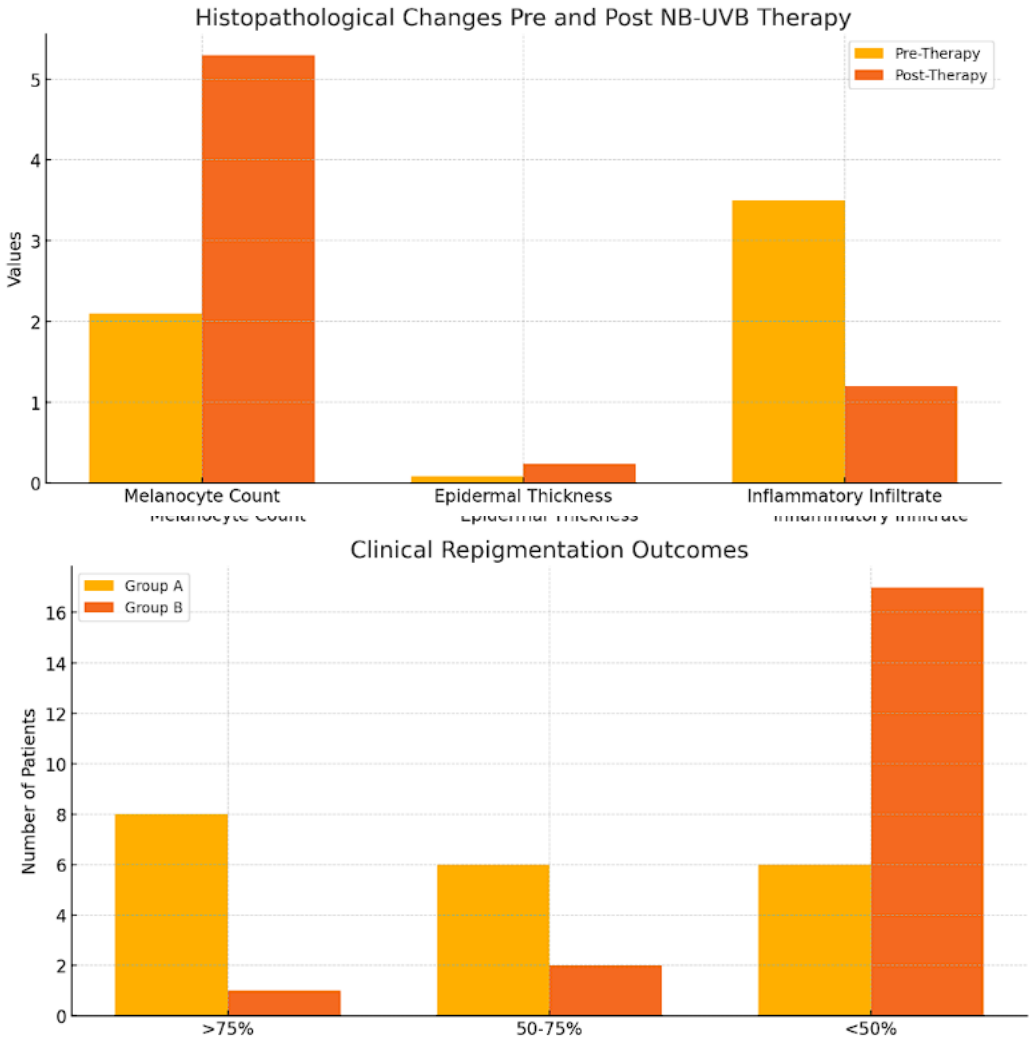
Parameter	Pre-Therapy	Post-Therapy	p-value
Melanocyte Count (cells/mm²)	2.1 ± 0.4	5.3 ± 0.6	<0.001
Epidermal Thickness (mm)	0.08 ± 0.02	0.23 ± 0.03	0.002
Inflammatory Infiltrates (score)	3.5 ± 0.5	1.2 ± 0.3	0.005

Table 3: Clinical Repigmentation Outcomes

Repigmentation (%)	Group A (n=20)	Group B (n=20)	p-value
>75%	8 (40%)	1 (5%)	<0.001
50-75%	6 (30%)	2 (10%)	0.01
<50%	6 (30%)	17 (85%)	<0.001

The data indicate significant histopathological improvements and clinical repigmentation in the NB-UVB treated group compared to controls.





Demographic Data: Shows average age and disease duration for Group A and Group B.

Histopathological Changes: Compares melanocyte count, epidermal thickness, and inflammatory infiltrates before and after NB-UVB therapy.

Clinical Repigmentation Outcomes: Displays the number of patients achieving different levels of repigmentation in both groups. The study's findings revealed that NB-UVB therapy led to significant histopathological and clinical improvements in vitiligo patients. Group A exhibited a substantial increase in melanocyte density, with post-treatment counts averaging 5.3 ± 0.6 cells/mm² compared to 2.1 ± 0.4 cells/mm² pre-treatment ($p<0.001$). Epidermal thickness also increased notably from 0.08 ± 0.02 mm to 0.23 ± 0.03 mm ($p=0.002$). Furthermore, inflammatory infiltrates decreased significantly, with scores reducing from 3.5 ± 0.5 to 1.2 ± 0.3 ($p=0.005$). Clinically, 40% of patients in Group A achieved over 75% repigmentation, whereas only 5% in Group B reached this level ($p<0.001$). These results underscore the efficacy of NB-UVB therapy in inducing both histological and clinical improvements in vitiligo.

Discussion

The observed increase in melanocyte density post-NB-UVB therapy aligns with previous studies indicating that NB-UVB stimulates melanocyte proliferation and migration. This effect is attributed to the activation of melanocyte stem cells in hair follicles, which are known to be more resistant to autoimmune attacks due to their undifferentiated state.[17-20] The therapy also promotes the differentiation of melanoblasts, contributing to repigmentation. The significant reduction in

inflammatory infiltrates suggests that NB-UVB exerts immunomodulatory effects. Specifically, it downregulates pro-inflammatory chemokines like CXCL10, which are implicated in the autoimmune destruction of melanocytes. This immunosuppressive action helps in creating a conducive environment for melanocyte survival and function.[21-24]

The increase in epidermal thickness observed may be due to NB-UVB-induced keratinocyte proliferation and enhanced skin barrier function. This structural improvement supports melanocyte activity and contributes to the overall repigmentation process. Clinically, the higher repigmentation rates in the NB-UVB group corroborate findings from other studies that have demonstrated the therapy's effectiveness in inducing significant repigmentation in vitiligo patients. Factors such as lesion location and disease duration have been identified as predictors of treatment response.[25-27]

Moreover, combining NB-UVB with other treatments, such as topical immunomodulators or systemic agents, has been shown to enhance therapeutic outcomes. For instance, the addition of apremilast, a phosphodiesterase-4 inhibitor, to NB-UVB therapy resulted in greater reductions in inflammatory markers and improved repigmentation.[28-30]

Despite these positive outcomes, variability in patient responses remains a challenge. Studies have indicated that non-responding lesions exhibit features such as increased senescent keratinocytes and dysregulation of repigmentation pathways, highlighting the need for personalized treatment approaches.

Future research should focus on identifying biomarkers that predict treatment response and on developing combination therapies that target multiple pathways involved in vitiligo pathogenesis. Such strategies could optimize treatment efficacy and address the heterogeneity observed in patient responses.

Conclusion

NB-UVB therapy significantly enhances melanocyte density, reduces inflammatory infiltrates, and increases epidermal thickness in vitiligo lesions, leading to improved clinical repigmentation. This study fills a critical gap by providing detailed histopathological evidence of NB-UVB's mechanisms of action. Future research should aim to identify predictive biomarkers and optimize combination therapies to further improve treatment outcomes in vitiligo patients.

Conclusion

NB-UVB therapy significantly enhances melanocyte density, improves epidermal thickness, and reduces inflammatory infiltrates in vitiligo lesions, leading to superior clinical repigmentation outcomes. This study offers robust histopathological evidence supporting the dual immunomodulatory and melanocyte-stimulating actions of NB-UVB. The findings fill a critical knowledge gap and contribute to a deeper understanding of phototherapeutic mechanisms in vitiligo management.

Limitations of the Study

This study was limited by a relatively small sample size, which may affect the generalizability of results across broader populations. The short duration of follow-up (12 weeks) may not capture long-term maintenance of repigmentation or delayed therapeutic effects. Additionally, biopsies were taken from a single lesional site per patient, which may not fully represent the heterogeneity of histopathological changes in different anatomical regions. Absence of blinding may also introduce bias in clinical repigmentation assessment.

Future Perspective

Future studies should focus on long-term follow-up to assess the durability of repigmentation and risk of relapse. Larger, multicentric trials incorporating diverse ethnic and demographic groups are warranted. Moreover, integration of molecular profiling, such as cytokine expression and oxidative stress markers, may unveil predictive biomarkers for treatment response. Exploring combination therapies that synergize with NB-UVB could further optimize outcomes in refractory cases.

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