

Oxidative Stress Levels in Relation to Vitiligo Severity and Activity

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Background: Several theories suggest melanocyte death in vitiligo, such as the oxidative stress theory. Vaspin is a steady marker for the assessment of the oxidative stress events. Narrow-band ultra-violet B (NB-UVB) therapy has developed vaspin in psoriasis and atopic dermatitis; but there is a little information on the impact in vitiligo and the association among vaspin rates and severity of disease and repigmentation. The relationship among serum vaspin levels and activity of vitiligo and its severity remained controversial.

Objective: Investigating NB-UVB photo-therapy effect on vaspin in Vitiligo cases.

Patients and Methods: In 56 vitiligo patients, serum vaspin levels had been measured before and following presentation in 48 NB-UVB sessions. Base-line vaspin rates of patients were compared to control rates for the stable participants of age and gender. Vitiligo region index (VASI) scoring method was used to test clinical response.

Results: The mean vaspin serum in the controls was significantly lower ($P < 0.001$). A substantial increase in Vaspin ($P < 0.001$) was observed following photo-therapy. The elevation in vaspin was adversely correlated with base-line vaspin levels. Also, there has been a significant correlation among vaspin levels and the severity index for Vitiligo Region (VASI).

Conclusion: NB-UVB enhancement of vitiligo is accompanying with an up-regulation of serum vaspin records. We, consequently, believe that vaspin has a significant function in the pathogenesis of vitiligo and contributes to its therapeutic effectiveness.

Keywords: Vaspin; Vitiligo; VASI; Ultraviolet B Photo-therapy

Abbreviation

NB-UVB: Narrow Band Ultraviolet B; VASI: Vitiligo Area Severity Index; IL: Interleukin; TNF: Tumor Necrosis Factor

Introduction

Vitiligo, the most frequent attained diversity of leukoderma, influences about 0.5% - 2% of the universal general populace, irrespective of ethnic origin or race, and reasons substantial social and psychological complications in all impacted cases [1].

Because of its multi-factorial properties, the pathogenesis of vitiligo is poorly well-known [2]. Several pathogenic concepts were suggested, involving autoimmune, cytotoxic, and oxidant-antioxidant mechanisms, in addition to an intrinsic defecting of melanocytes [3]. As well, in segmental vitiligo, a neural hypothesis was assumed. While all these theories are gorgeous, vitiligo is frequently a consequence of the conjunction of various ones [4]. The hallmark of vitiligo is the existence of mutilating white skin patches as a consequence of epidermal melanocyte damages [5].

Vaspin is a serine protease inhibitor of the serpin own group [6]. Formerly recognized in white adipose tissues, vaspin was proposed to characteristic as an adipokine and seems to have advantageous results on the pathogenesis of auto-inflammatory disorders [7,8].

We found, no any preceding study that compared the influence of NB-UVB on tissues levels of vaspin in vitiligo cases. Consequently, this current work aimed to calculate the serum vaspin levels earlier and afterward the usage of NB-UVB in vitiligo cases.

Materials and Methods

The current work was performed on cases with vitiligo who admitted the photo-therapy unit of the Dermatology Department at Zagazig University Hospitals within the interval from July 2019 to April 2020. Pregnant females, cases younger than 6-yrs, cases with a history of photo-sensitivity or photo-mediated diseases, and cases managed by receiving photo-therapy in the last 3-mths have been omitted from this work.

56-cases have been registered in this work, they were (26 males and 30 females) have been present for final evaluation. Their ages ranging between 15 to 57-yrs. 14 cases (25%) were of kind III skin, 28 (50%) were of kind IV skin, and the residual cases (25%) of kind V skin.

At the primary visit, complete history-take, generalized examinations, and localized examinations have been performed for all cases, and disorder severity and extent have been evaluated via the vitiligo area severity index (VASI scoring). Ages, gender, period of vitiligo, family history of vitiligo, and Fitzpatrick skin photo-type have been documented.

All cases have been managed with NB-UVB irradiating, that was accomplished in a Waldmann UV-100 I photo-therapy cabin (Waldmann Medizintechnik, Schweningen, Germany), prepared with UVB TL-01 tubes (Philips TL-01, Japan; Eindhoven, the Netherlands) with a wavelengths between 310 to 315 nm and a highest one of 311 nm [9].

Photo-therapy was started at a dosage of 0.2 J/cm² for cases with skin photo-types I or II and a dosage of 0.3 J/cm² for skin photo-types III to Consequently, the dosage was elevated by 20% for each session after which stabilized while minimum erythema improved. Treating sessions have been carried out two times every

week on un-consecutive days with protective of genitals and eyes until they have been influenced by vitiligo. Within therapy, the cases have been often assessed for erythema, respond to therapy, and any side effect. In case of extreme erythema with burns and pains, therapy was discontinued till the resolution of signs and resumed afterward on the final allowed dosage [10].

Pictures of the body locations impacted by vitiligo have been recorded for every case at base-line and after 2-yrs (forty-eight therapies) for assessment of medical reaction the usage of a Sony camera (12 megapixels; Japan). The vitiligo area scoring index (VASI) was employed for the severity evaluation and extension of vitiligo and to evaluate the medical development. VASI was estimated at base-line and the stop of forty-eight NB-UVB sessions. It is built on the valuation of the region of vitiligo patches and the extension of regimentation in those patches through time [11].

The evaluations were performed in 5 body areas: hands, feet, trunk, higher and lower extremities. For every area, the VASI was accounted as the outcome the area of vitiligo in hand units (B1% of the entire body superficial region per unit) and the grade of skin depigmentation in every hand unit measured patch (expressed via percent of 0, 10, 25, 50, 75, 90, or 100%). The face and neck regions have been evaluated distinctly. The overall body VASI was then determined via the subsequent formula:

$$\text{VASI} = \sum \text{All body locations (hand units)} \times (\text{remaining depigmentation}) \quad [12]$$

Blood specimens have been collected earlier than beginning of photo-therapy and afterward publicity to 48 sessions of NB-UVB radiation. Serum vaspin was additionally evaluated controls with analogous ages and genders without any family history of vitiligo, to be as matched with base-line degrees in vitiligo cases.

Measurement of serum vaspin degrees

Definite enzyme-related immune-sorbent assay kits have been employed to evaluate serum vaspin degrees (Bio-Vendor Lab. Medicine, Czech Republic). Shortly, 96-properly polystyrene sheets covered with antivaspin antibody have been hatched with 3-times dilute serum at normal temp. for 1 hour. Then cleaning the well, a biotinlabeled poly-clonal antivaspin anti-body was supplemented and hatched with the taken vaspin for 1 hour. Subsequently, the

wells have been cleaned and hatched at room-temp. for 30-mins with horseradish peroxidase-conjugated streptavidin. Next, the wells have been washed once more, tetramethyl-benzidine was supplemented and hatched at room temp. for 10 minutes. Eventually, H₂SO₄ was delivered to terminendate the reaction, and absorbing at 450 nm was determined. Serum vaspin levels have been determined via a reference curve.

Results

In the current work 56 cases have been enrolled (26-men and 30-women, with ages between 15 and 57-yrs. The base-line demographical characteristics and disorder features of cases who accomplished this work are presented in table 1.

Table 1: Demographic and clinical features of studied groups. IQR, Interquartile Range.

	Patient (56)	Control	P-value
Age (years)			
Mean ± SD	34.73 ± 12.08	27.67 ± 16.42	0.16*
Male [n (%)]	8 (36.4)	5 (83.3)	0.07z
Fitzpatrick skin type [n (%)]			
III	14 (25.0)	20 (35.7)	0.28z
IV	28 (50.0)	18(32.1)	
V	14 (25.0)	18(32.15)	
Duration of disease (years) Median (IQR) (range)	6 (10.8) (0.3-20)	N/A	
Extent of vitiligo (VASI) (%) Median (IQR) (range)	2.7 (5.5) (0.62-54.2)	N/A	
Positive family history [n (%)]	15 (27.3)	0 (0)	0.37z

*Student’s t-test was used to compare the mean difference between the two groups. zw2-Analysis was used to compare the difference in proportions. The Mann–Whitney U-test was used to compare the median difference between the two groups.

Base-line serum vaspin counts of cases were matched with those of 40 analogous controls. The mean serum vaspin was significantly lower in cases in comparison to control group (99.72 ± 12.11 vs. 257.34 ± 28.11, respectively; P-value < 0.001).

A nonsignificant association was found among the base-line vaspin level and other variables, involving ages, skin kind, period, and base-line VASI scoring.

Regarding the medical responding to photo-therapy, a significant development was found in VASI scores from a median of 2.7% (ranging from 0.62 to 54.25) at base-line to a median of 1.8% (ranging from 0.34 to 45) afterward 48-sessions (P-value < 0.001). The median development in the VASI scores were 37.5%. The mean collective UVB dosage afterward 48-sessions were 31.96 ± 9.92 J/cm².

In Comparison to base-line, a significant rise was found in the mean serum concentrations of vaspin in cases afterward 48 NB-UVB sessions. Serum vaspin exhibited a significant rise (P-value < 0.001) subsequent to photo-therapy (Table 2 and Table 3).

Table 2: Vaspin levels in patients before NB-UVB compared to controls.

Vaspin P value	Patients before NB-UVB	Controls	P value
Range 257.34 ± 28.11	82.5-121.4 pg/mg 215.3-298.5 pg/mg < 0.001	215.3-298.5 pg/mg	< 0.001
Mean ± SD	99.72 ± 12.11	257.34 ± 28.11	

*P-value <0.05 is considered statistically significant.

Table 3: Vaspin levels and VASI in patients before and after NB-UVB.

	Patients before NBUVB	Patients after NBUVB	P value
Vaspin			
Range	82.50-121.40	142.60-241.60	< 0.001
Mean± SD	99.72 ± 12.39	190.92 ± 27.61	
VASI			
Range	3.2-11.7	1.7-6.7	< 0.001
Mean± SD	7.29 ± 2.99	3.25 ± 2.57	

*P-value <0.05 is considered statistically significant.

The base-line vaspin level shows a significant association with the base-line VASI scores. There was a high significant negative association among the percentage of VASI score change and both UVB dosage and percentage of vaspin change. Improvement (decrease) in the VASI score was correlated with a high UVB dosage and an increase in vaspin (Table 4).

Table 4: Correlations between Percentage of VASI score change and other variables.

UVB: Ultraviolet B; HS: High Statistical Significance; UVB: Ultraviolet B.

Variables	Percentage of VASI score change	
	r	p
Baseline VASI score	0.21	0.2
Baseline vaspin	0.31	0.06
UVB dose	- 0.6	<0.001 (HS)
Percentage of vaspin change	- 0.52	<0.001 (HS)

*P-value <0.05 is considered statistically significant.

Discussion

The inculcation of vaspin in the complicated pathogenesis of vitiligo has got more ground over the earlier ages, as many investigations [13], the present one, reported the significantly lower concentrations of vaspin between the vitiligo cases compared with the control group.

The present work is the 1st to investigate the impact of NB-UVB on the productions of vaspin in the influenced vitiligo cases. The outcomes of this work revealed that the vaspin counts were significantly elevated afterward management with NB-UVB photo-therapy.

The present work may be attributed to various issues. First, vaspin employs anti-inflammatory influences via rise expressions of the proinflammatory adipokines, like resistin and leptin [14]. Furthermore, it dampens IL-1β persuaded expressions and secretions of proinflammatory cytokines, like IL-6, IL-8, and monocyte chemoattractant protein-1 (MCP1) and TNFα as well as decreasing cytokine-persuaded activating of the intra-cellular and proinflammatory NFκB gesturing cascades (IKKα/β, IκB, and NFκB) [14,15].

Vaspin not only may be employed as a biomarker of the disorder but as well might mirror the disorder severity. In this work, vaspin concentrations were considerably upregulated in cases afterward 48-sessions of NB-UVB with major development in VASI scoring afterward therapy (P-value < 0.001).

Conclusion

Development of vitiligo by NB-UVB is accompanied with up-regulation of serum vaspin level. Consequently, we propose that vaspin had significant roles in vitiligo pathogenesis.

Conflict of Interest Statement for All Authors

No conflict of interest.

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Bibliography

1. Ezzedine K and Silverberg N. "A practical approach to the diagnosis and treatment of vitiligo in children". *Pediatrics* 138.1 (2016): e20154126.
2. van den Boorn JG., et al. "Autoimmune destruction of skin melanocytes by perilesional T cells from vitiligo patients". *Journal of Investigative Dermatology* 129 (2009): 2220-32.
3. Tembhre MK., et al. "T helper and regulatory T cell cytokine profile in active, stable and narrow band ultraviolet b treated generalized vitiligo". *Clinica Chimica Acta* 424 (2013): 27-32.
4. Esmat S., et al. "Photo-therapy: The vitiligo management pillar". *Clinics in Dermatology* 34.5 (2016): 594-602.
5. Dillon AB., et al. "Advances in Vitiligo: An Update on Medical and Surgical Treatments". *Journal of Clinical and Aesthetic Dermatology* 10.1 (2017): 15-28.
6. Saalbach A., et al. "Vaspin—a link of obe-sity and psoriasis?" *Experimental Dermatology* 21.4 (2012): 309-312.
7. Phalitakul S., et al. "Vaspin prevents TNF-alpha-induced intracellular adhesion molecule-1 via inhibiting reactive oxygen species-dependent NF-kappa B and PKC theta activation in cultured rat vascular smooth muscle cells". *Pharmacology Research* 64.5 (2011): 493-500.
8. Saalbach A., et al. "Anti-inflammatory action of keratinocyte-derived vaspin: relevance for the patho-genesis of psoriasis". *American Journal of Pathology* 186.3 (2016): 639-651.

9. Bae J., *et al.* "Photo-therapy for Vitiligo: A Systematic Review and Meta-analysis". *JAMA Dermatology* 153.7 (2017): 666-674.
10. Park JH., *et al.* "Efficacy of narrow-band UVB photo-therapy in vitiligo patients". *Korean Journal of Dermatology* 41.8 (2003): 1022-1027.
11. Kawakami T and Hashimoto T. "Disease Severity Indexes and Treatment Evaluation Criteria in Vitiligo". *Dermatology Research and Practice* (2011).
12. Hamzavi I., *et al.* "Parametric modeling of narrowband UV-B photo-therapy for vitiligo, using a novel quantitative tool: the Vitiligo Area Scoring Index". *Archives of Dermatology* 140.6 (2004): 677-683.
13. Zieger K., *et al.* "Vaspin suppresses cytokine-induced inflammation in 3T3-L1 adipocytes via inhibition of NFκB path-way". *Molecular and Cellular Endocrinology* 460 (2018): 181-188.
14. Kiluk P., *et al.* "Role of omentin and vaspin in metabolic diseases in association with psoriasis". *Przegląd Dermatologiczny* 104 (2017): 519.
15. Li YL., *et al.* "Proteomic Analysis of the Serum of Patients with Stable Vitiligo and Progressive Vitiligo". *Chinese Medical Journal (Engl)*. 131.4 (2018): 480-483.