



Down-regulation of tissue levels of serine protease inhibitor (vaspin) in psoriasis vulgaris patients: a possible mechanism of narrowband ultraviolet B radiation

Khadiga Sayed Sayed¹ · Eman Raafat Said¹ · Faisal Nouredin Mohammed² · Mira Algorhary¹ · Laila Ahmed Rashed³

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Abstract

Vaspin is a serine protease inhibitor of the serpin family which has an anti-inflammatory effect. It has an important role in the pathogenesis of some inflammatory diseases such as psoriasis. There are no previous studies comparing the effect of narrowband ultraviolet B (NB-UVB) radiation on tissue vaspin levels in psoriasis. So we aimed in this case–control study to estimate the possible role of vaspin in the pathogenesis of psoriasis, and to evaluate the effect of NB-UVB radiation on tissue vaspin in psoriasis. This study included 21 non-obese patients with moderate psoriasis and 20 non-obese clinically healthy age and sex matched controls. Patients underwent 24 sessions of NB-UVB radiation. A 4 mm punch skin biopsy was taken from all patients before and after treatment and from the controls for estimation of tissue vaspin level by enzyme-linked immunosorbent assay. Vaspin levels was significantly lower in patients before NB-UVB ($99.72 \text{ pg/mg} \pm 12.11 \text{ pg/mg}$) compared to controls ($257.34 \text{ pg/mg} \pm 28.11 \text{ pg/mg}$) with ($P < 0.001$). In addition, high significant difference was detected between vaspin levels in patients before ($99.72 \text{ pg/mg} \pm 12.39 \text{ pg/mg}$) and after NB-UVB ($190.92 \text{ pg/mg} \pm 27.61 \text{ pg/mg}$) with ($P < 0.001$). In conclusion, improvement of psoriatic plaques by NB-UVB is associated with an upregulation of tissue vaspin levels. Therefore, we suggest that vaspin has an important role in psoriasis pathogenesis.

Keywords Psoriasis vulgaris · NB-UVB · Adipokines · Vaspin

Introduction

Psoriasis vulgaris is a common inflammatory disorder, affecting between 1 and 3% of the population. The disease is characterized by sharply demarcated, red papules and plaques covered with silvery laminated scales [11]. Psoriasis is believed to be a Th1/Th17 mediated inflammatory disease [4, 13].

Over the previous decades, it has been argued whether psoriatic skin lesions arise from a primary alteration in epidermal keratinocytes (KCs) or in immunocytes [3]. KCs

secrete cytokine and chemokines that recruit and activate various immune cells, which in turn lead to the production of cytokines that support KCs activation, proliferation, and differentiation. Disturbed balance of this cross talk between epidermal KCs and immunocytes is believed to contribute to the pathogenesis of chronic inflammatory skin diseases among them is psoriasis [9].

KCs are a rich source of the serpin protease inhibitor vaspin (serpinA12) which was originally described as an adipokine in adipose tissue. The expression of vaspin in KCs correlates with KC differentiation [15]. Previous studies demonstrated significant down-regulation of epidermal vaspin in human psoriasis [2, 14, 15].

Narrowband ultraviolet B (NB-UVB) radiation is an effective treatment for psoriasis which reverses several pathological alternations found in the disease such as its suppressive immunomodulatory effect on expression of cytokines released by Th1 and Th17 cells [5]. The immunomodulatory effects of UVB on cutaneous inflammatory responses are well reported but their exact mechanisms are poorly understood [10].

✉ Eman Raafat Said
dremy1983@gmail.com; dremy07@cu.edu.eg

¹ Dermatology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

² Dermatology and Venereology Department, National Research Center, Giza, Egypt

³ Biochemistry Department, Faculty of Medicine, Cairo University, Cairo, Egypt

To our knowledge, there are no previous studies comparing the effect of NB-UVB on tissue level of vaspin in psoriasis vulgaris patients. Therefore, the aim of this study is to measure tissue vaspin levels before and after using NB-UVB in psoriasis vulgaris patients.

Patients and methods

This case–control study was approved by Dermatology Research Ethical committee, Faculty of medicine, Cairo University. All subjects signed informed written consent to participate in this study. This study was conducted on 21 non-obese (body mass index < 30) patients with moderate to severe psoriasis vulgaris (BSA > 10, PASI > 10, DLQI > 10) collected from Kasr Al Ainy hospital psoriasis clinic in Dermatology department, Faculty of medicine, Cairo University. Erythrodermic or pustular psoriasis, pregnant, and lactating females, patients with malignant or autoimmune diseases or diabetes mellitus and patients who took systemic or active topical therapy for psoriasis at least 4 weeks prior to inclusion in this study were excluded.

All patients were subjected to detailed history taking (including: duration of the disease, family history of psoriasis, history of associated comorbidities and history of previous medications), clinical assessment to determine the extent of disease (BSA %) using rule of nine [18] and assessment of disease severity using Psoriasis Area and Severity Index (PASI) score [6]. A 4 mm punch skin biopsy was taken from each patient from a defined psoriatic plaque before and after 24 sessions of NB-UVB (3 times weekly) from the same plaque (or same location if cured), and from an area of normal skin of each individual of the control group trying to match the site as possible, for estimation of tissue vaspin level.

UVB radiation was delivered in lighting cabins (Waldmann TL01; Herbert Waldmann GmbH & Co. KG, Villingen-Schwenningen, Germany) equipped with the UV lamps (TL01–16; Philips), which emitted UVB rays in the wavelength range of 311–313 nm (with 311 nm peak emission). All patients started UVB treatment at 0.21 J/cm², then the dose was increased gradually according to the patient's response until the minimal erythema dose was reached.

Measurement of tissue vaspin level by enzyme-linked immunosorbent assay (ELISA)

The tissues were minced into small pieces and rinsed in ice-cold PBS (0.01 M, pH 7.4) to remove excess blood thoroughly. Tissue pieces were weighed and then homogenized in PBS [tissue weight (g): PBS (mL) volume = 1:9] with a

glass homogenizer on ice. To further breakdown the cells, the suspension was sonicated with an ultrasonic cell disrupter or subjected to freeze–thaw cycles. The homogenates were then centrifuged for 5 min at 5000 × g to get the supernatant. The supernatant was kept frozen at 70 °C till analysis by ELISA technique using human vaspin ELISA kits (Elabscience, USA). Catalog No: E-EL-HI762.

The collected data were coded, tabulated, and statistically analyzed using IBM Statistical Package for Social Sciences (SPSS) software version 18.0, IBM Corp., Chicago, USA, 2009.

Results

The current study included 21 non obese patients with psoriasis vulgaris as well as 20 age and sex matched non obese controls. No statistically significant difference was detected between patients and controls regarding age ($P=0.835$) and sex ($P=0.901$). Demographic and clinical characteristics of included patients and controls are presented in Table 1.

Vaspin levels in patients before NB-UVB (99.72 pg/mg ± 12.11 pg/mg) was found to be significantly lower compared to its levels in controls (257.34 pg/mg ± 28.11 pg/mg) ($P < 0.001$) (Table 2 and Fig. 1). In addition, a significant difference was detected between vaspin levels in psoriatic patients before (99.72 pg/mg ± 12.39 pg/mg) and after NB-UVB (190.92 pg/mg ± 27.61 pg/mg) with up-regulated levels ($P < 0.001$) (Table 3 and Fig. 2). A statistically significant reduction of PASI after NB-UVB was detected ($P < 0.001$) (Table 3 and Fig. 3).

Positive correlation was detected between vaspin after NB-UVB and age of patients. No other correlation was detected between vaspin and any other data of the patients (sex, family history, duration of disease, comorbidities, extent, PASI). No correlation was detected between change in vaspin and change in PASI.

Discussion

The incrimination of vaspin in the complex pathogenesis of psoriasis has gained much ground over the past years, as several studies [1, 14, 15], among which is the current one, documented the significantly lower levels of vaspin among the psoriatic patients in comparison to the controls. Taking matters a step further, the current study is the first to study the effect of NB-UVB on the production of vaspin in the affected skin of psoriatic patients. The results of our study demonstrated that the tissue vaspin levels were significantly increased after treatment with NB-UVB phototherapy.

Table 1 Demographic and clinical data of patients and controls

	Patients	Controls	<i>P</i> value
Number	21	20	
Age			
Range	19–63 years old	21–56 years old	0.835
Mean ± SD	39.81 ± 14.8	38.95 ± 8.85	
Sex			
Males	13 (61.9%)	12 (60%)	0.901
Females	8 (38.1%)	8 (40%)	
Duration of disease (years)			
Range	0.5–28		
Mean ± SD	7.82 ± 7.9		
Extent (% BSA)			
Range	12–80		
Mean ± SD	39.81 ± 22.73		
PASI before NB-UVB:			
Range	10–40.3		
Mean ± SD	19.83 ± 7.54		
Co-morbidity			
Hypertension count	1		
%	4.8%		
Hypothyroidism count	1		
%	4.8%		
Family history			
Positive count (%)	2 (9.5%)		
Negative count (%)	19 (90.5%)		

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

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

The possible role of vaspin in psoriasis documented in the current study can be attributed to several factors. First, vaspin exerts anti-inflammatory effects through increase expression of the pro-inflammatory adipokines, such as resistin and leptin [7, 12]. Moreover, it blunts IL-1β induced expression and secretion of pro-inflammatory cytokines, such as IL-6, IL-8, and monocyte chemoattractant protein-1 (MCP1) and TNFα in addition to reducing cytokine-induced activation of the intracellular and pro-inflammatory NFκB signaling cascades (IKKα/β, IκB and NFκB) [19].

Second, vaspin expression is associated with improved epidermal differentiation, with low levels in proliferating KCs and high levels in differentiated cells through the expression of differentiation-associated genes [15].

The lack of significant association in the current study between the vaspin level and the PASI does not abort the

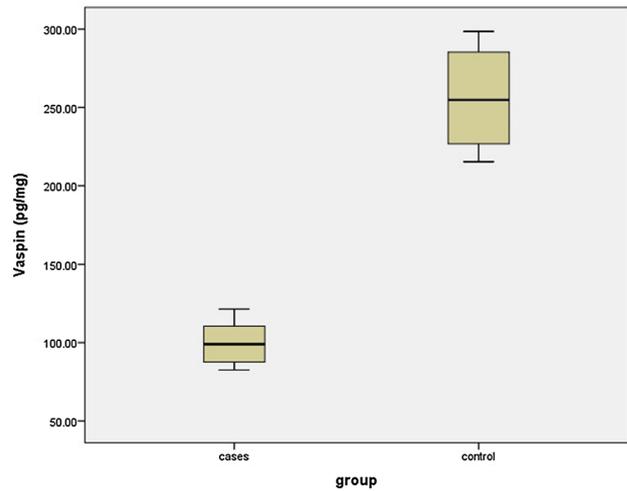


Fig. 1 comparison between vaspin in patients before NB-UVB and controls

Table 3 Vaspin levels and PASI in patients before and after NB-UVB

	Patients before NB-UVB	Patients after NB-UVB	<i>P</i> value
Vaspin			
Range	82.50–121.40	142.60–241.60	<0.001
Mean ± SD	99.72 ± 12.39	190.92 ± 27.61	
PASI			
Range	10.00–40.30	0.1–29.60	<0.001
Mean ± SD	19.83 ± 7.54	8.02 ± 8.53	

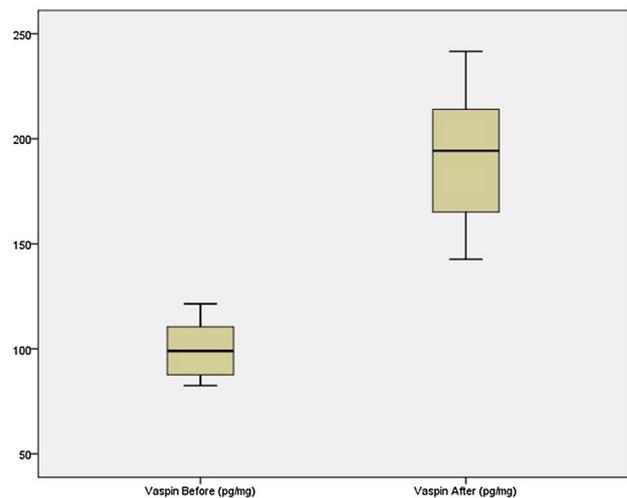


Fig. 2 comparison between vaspin in patients before and after NB-UVB

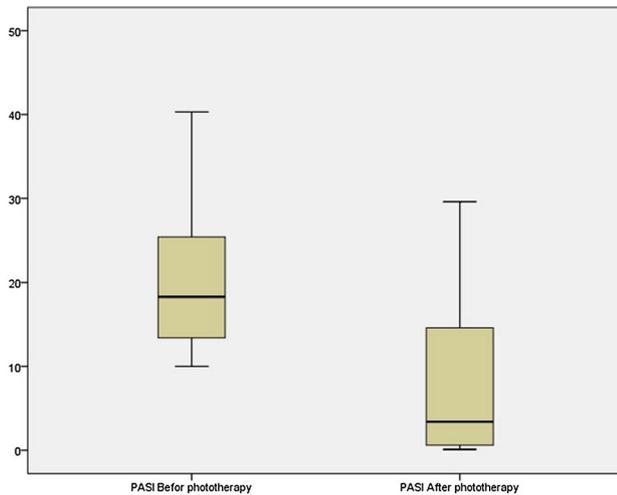


Fig. 3 comparison between PASI of patients before and after NB-UVB

important role played by vaspin in the pathogenesis of psoriasis, but can be attributed to the multifactorial nature of the disease. Ataseven and Kesli [1] suggested that vaspin not only can be used as a marker of the disease but also may reflect the severity of disease.

In our study vaspin tissue levels were significantly upregulated in patients after 24 sessions of NB-UVB with significant improvement in PASI score after treatment ($P < 0.001$).

Some studies investigated other adipokines before and after NB-UVB as Shibata et al. [16], who investigated serum adiponectin and IL-6 levels in 6 patients with psoriasis vulgaris before and after (NB-UVB) irradiation using ELISA technique. They observed upregulation of adiponectin levels after treatment.

The study of Kawashima et al. [8], investigated serum resistin and leptin levels before and after bath-psoralen and ultraviolet (UV) A or narrow band UVB therapy using enzyme-linked immunosorbent assay. Phototherapy induced no remarkable change in the leptin levels, but significantly decreased serum resistin levels. The reduction in serum resistin induced by phototherapy might be related to the clinical efficacy of this treatment for psoriasis.

Takahashi et al. [17] demonstrated that improvements of serum levels of adiponectin, leptin, and resistin are linked to successful treatment of psoriasis by NB-UVB. To the best of our knowledge, no published work to date has investigated the effect of NB-UVB on vaspin production in lesional skin of psoriatic patients.

In our study, comparison of tissue vaspin levels before and after therapy between the two sexes, showed no statistically significant differences. This means that the vaspin

production in psoriatic patients was not affected by the hormonal factors due to sex difference.

Limitation

- Small number of patients enrolled in our study; we recommend that further large scale studies evaluate the vaspin levels following other forms of phototherapy modalities as PUVA and BB-UVB.

Conclusion

Improvement of psoriatic plaques by NB-UVB is associated with an upregulation of tissue vaspin levels. Therefore, we suggest that vaspin has an important role in psoriasis pathogenesis.

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Compliance with ethical standards

Conflict of interest The author(s) declare that they have no competing interests.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the research ethical committee (REC) of Dermatology Department, Faculty of medicine, Cairo University which is organized and operated according to the declaration of Helsinki for human subject researcher 2013.

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