The effect of narrow-band ultraviolet-B phototherapy on soluble intercellular adhesion molecule-1 and soluble E-selectin in psoriasis vulgaris patients
Ahmed A. Saleha, Jehan H. Sabry, Neveen E. Sorour

Introduction
The pathogenesis of psoriasis is multifactorial, with genetic, environmental, and immunological factors contributing to the disease [1]. It includes excessive proliferation and altered differentiation of epidermal keratinocytes, mediated by the immune system and characterized by a dense inflammatory infiltrate composed of clusters of CD4+ Th cells and antigen-presenting dendritic cells in the dermis and CD8+ T cells and neutrophils in the epidermis [2]. Also, there is increased expression of adhesion molecules such as intercellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1, and E-selectin [3]. ICAM-1 is an immunoglobulin-like adhesion molecule that is expressed on the surface of several cell types, including endothelial cells and cells involved in the immune response [4]. It plays a role in transendothelial migration and adhesion processes involved in the pathogenesis of psoriasis, through interaction with lymphocyte function-associated antigen-1, leading to the entry of T cells into the epidermis [5]. The molecule of E-selectin mediates adhesive contacts between blood cells and vessel walls. These interactions are loose and reversible, operate under conditions of shear flow, and result in leukocyte rolling along the vessel wall [6].

Background
Increased levels of soluble E-selectin (sE-selectin) and soluble intercellular cell adhesion molecule-1 (sICAM-1) have been reported in patients with psoriasis vulgaris compared with controls.

Objective
The aim of this study was to investigate the effects of narrow-band ultraviolet-B (NB-UVB) phototherapy on sE-selectin and sICAM-1 serum levels in patients with psoriasis vulgaris.

Patients and methods
This case–control study included 30 patients with psoriasis vulgaris and 20 apparently healthy participants as a control group. Both patients and controls were subjected to full history taking, dermatological examination, and measurement of sE-selectin and sICAM-1 using enzyme-linked immunosorbent assay kits. In the patient group, sE-selectin and sICAM-1 were measured after treatment with NB-UVB phototherapy, and the response was assessed by the Psoriasis Area and Severity Index (PASI) score. sE-selectin and sICAM-1 serum levels were compared before and after treatment and correlated with PASI scores.

Results
In this study, sE-selectin and sICAM-1 serum levels were significantly higher in the patient group than in the control group (P = 0.001 for both). There were statistically significant reductions in sE-selectin and sICAM-1 serum levels after NB-UVB phototherapy (P = 0.001 for both), but still the levels were higher than those of controls. PASI scores significantly decreased after treatment, confirming the efficacy of NB-UVB phototherapy. Both sE-selectin and sICAM-1 serum levels were positively correlated with PASI scores before and after NB-UVB phototherapy (P = 0.001 for both).

Conclusion
The present study emphasizes the complex nature of the roles played by cell adhesion molecules in the immune-pathogenesis of psoriasis and the effect of NB-UVB phototherapy on their values in relation to the PASI score. Also, results of this study provide a rationale for the possible application of sE-selectin and sICAM-1 measurements as biomarkers of psoriasis activity and predictors of possible exacerbation.

Keywords: narrow-band ultraviolet-B, Psoriasis Area and Severity Index, psoriasis vulgaris, soluble cell adhesion molecule-1, soluble E-selectin
processes involving activation of or damage to cells such as platelets and the endothelium [7].

sICAM-1 promotes angiogenesis and serves as an indicator of vascular endothelial cell activation or damage [8,9]; it also functions as an inhibitor of transmembrane ICAM-1-mediated activities, such as monocyte adhesion to activated endothelial cells [10], sE-selectin is regarded as an adequate marker of endothelial activation [7] and suppresses leukocyte migration by competing with surface-associated E-selectin, and can activate neutrophils and act as a proinflammatory agent [11]. Narrow-band ultraviolet-B (NV-UVB) phototherapy is of proven efficacy in the short-term treatment of moderate and extensive plaque psoriasis [12]. Despite its widespread use, there is little published literature on its impact on sCAMs.

The aim of this study was to investigate the effects of NB-UVB phototherapy on sE-selectin and sICAM-1 serum levels in patients with psoriasis vulgaris.

Patients and methods

Thirty patients with psoriasis vulgaris were recruited from the Outpatient Clinic of Benha University Hospital and 20 healthy participants served as controls during the period from September 2011 to August 2012. Written informed consent was obtained from all patients and controls before the study. The study was approved by the Research Ethics Committee of the Faculty of Medicine in Benha University. Inclusion criteria were patients with psoriasis vulgaris with at least 20% of their total body surface area involvement and Fitzpatrick skin types III and IV. Their age ranged between 15 and 60 years. Exclusion criteria included patients who had been treated with oral steroids, oral retinoids, and immunosuppressants during the previous 3 months and topical steroids during the previous 4 weeks. Patients with a history of previous failure or intolerance to phototherapy and pregnant or lactating women were excluded.

All patients were subjected to the following: history taking including personal history, present history with special emphasis on the onset, the course, and the duration of psoriasis, and history of previous or current treatment for psoriasis and date of stopping the drug. History of other systemic or skin diseases was also taken into account.

Narrow-band ultraviolet-B phototherapy protocol

All patients were irradiated with Waldmann UV 7001 K light stand (Medizinische Technik, Villingen-Schwenningen, Germany) with Philips TL-01 lamps (312 nm; Philips, Eindhoven, the Netherlands) after determining the 24-h minimal erythema dose. They were treated three times a week with a starting dose according to the skin photo type: skin type III was started with an initial UVB dose of 260 mJ/cm², and then increased by 40 mJ/cm² after each treatment. Skin type IV was started with an initial UVB dose of 330 mJ/cm², and then increased by 45 mJ/cm² after each treatment. In both skin types, the maximum UVB dose should not exceed 3000 mJ/cm² [13]. The treatment continued until clearance of all exposed psoriatic lesions or five consecutive sessions resulted in no further improvement and the patient had at least 16 exposures. The efficacy of treatment was assessed by means of the Psoriasis Area and Severity Index (PASI) score before and after NB-UVB [14]. A score of 4 or less was defined as clear or almost clear [15].

Laboratory investigations

Sample collection

A 5 ml sample of untreated peripheral blood was obtained by cubital vein puncture from each patient before and after NB-UVB treatment, and from each control subject for comparison. Samples were incubated at room temperature for 30–45 min to coagulate. Samples were centrifuged for about 10–15 min at 3000 rpm. Serum was divided into two Eppendorfs and stored in small tubes at −20°C until analysis.

Determination of serum level

Serum levels of sICAM-1 and sE-selectin were evaluated using a commercial enzyme-linked immunosorbent assay kit. It is a quantitative measurement supplied by IDELISA sE-selectin and sICAM-1 ELISA kit (ID Labs Inc., London, Ontario, Canada).

Statistical analysis

Data collected were tabulated and analyzed using the Statistical Package for Social Science (version 16; SPSS Inc., Chicago, Illinois, USA). Presentation and analysis of the present study was conducted using the mean and SD, the χ²-test, and the Pearson correlation.

Results

Clinical results

This study was conducted as a case-control study that included 30 patients with psoriasis vulgaris involving at least 20% of their total body surface area. They included 16 female and 14 male patients, with their age ranging from 15–60 years, with a mean of 34.43 ± 17.7 years. The control group included 14 female and six male participants with their age ranging from 18 to 51 years, with a mean of 35.1 ± 9.65 years. There was no statistically significant difference between the
patient and the control groups regarding their age and sex \((P = 0.879 \text{ and } 0.239, \text{ respectively})\). Of the patients involved in the study, two patients achieved nearly complete clearance with PASI score of 4 or less and mean number of sessions 17.5 \(\pm\) 0.71, whereas 28 patients achieved variable degrees of improvement, with mean number of sessions 30.64 \(\pm\) 6.6. There was a statistically significant difference in the PASI scores before and after NB-UVB phototherapy \((P = 0.001; \text{ Table 1 and Figs 1 and 2})\).

**Lab results**

There was a statistically significant difference between the patient group before treatment and the control group regarding sICAM-1 and sE-selectin serum levels \((P = 0.001 \text{ for both})\) (Table 2).

Regarding the patient group, there was a statistically significant difference in sICAM-1 and sE-selectin serum levels before and after NB-UVB phototherapy \((P = 0.001 \text{ for both})\) (Table 3).

A significant positive correlation was found between PASI scores, sICAM-1, and sE-selectin serum levels before and after NB-UVB phototherapy (Tables 4 and 5).

**Discussion**

Before the onset of therapy, there was a statistically significant difference between patients and controls regarding sICAM-1 serum levels \((P = 0.001)\). These results agreed with Schopf \textit{et al.} \cite{16}, Krasowska \textit{et al.} \cite{17}, Gangemi \textit{et al.} \cite{18}, Borskà \textit{et al.} \cite{19}, and Batycka-Baran \textit{et al.} \cite{20}. The same result was obtained with regard to sE-selectin serum levels \((P = 0.001)\), which agreed with studies that focused on the endothelial activity \cite{19–27}. In contrast, Ghalamkarpour \textit{et al.} \cite{28} found elevated serum levels of sE-selectin in psoriatic patients compared

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**Table 1** A comparison of PASI scores before and after NB-UVB phototherapy in the patient group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
<th>Paired t-test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI scores Before</td>
<td>16.32 ± 6.31</td>
<td>15.038</td>
<td>0.001*</td>
</tr>
<tr>
<td>After</td>
<td>5.067 ± 4.48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NB-UVB, narrow-band ultraviolet-B; PASI, psoriasis area and severity index. *P value <0.05 was considered significant.

**Table 2** A comparison between the patient and the control groups regarding sICAM-1 and sE-selectin serum levels before treatment

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Mean ± SD (ng/ml)</th>
<th>Student’s t-test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sICAM-1</td>
<td>Patients group</td>
<td>445.23 ± 76.3</td>
<td>9.89</td>
<td>0.001*</td>
</tr>
<tr>
<td>Control group</td>
<td>195.1 ± 38.58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sE-selectin</td>
<td>Patients group</td>
<td>5791.3 ± 2250.2</td>
<td>7.38</td>
<td>0.001*</td>
</tr>
<tr>
<td>Control group</td>
<td>477.42 ± 290.96</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

sE-selectin, soluble E-selectin; sICAM-1, soluble intercellular cell adhesion molecule-1. *P value <0.05 was considered significant.

**Table 3** A comparison of sICAM-1 and sE-selectin serum levels before and after NB-UVB phototherapy in the patient group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD (ng/ml)</th>
<th>Paired t-test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sICAM-1</td>
<td>Before</td>
<td>445.23 ± 76.3</td>
<td>7.911</td>
</tr>
<tr>
<td>After</td>
<td>339.1 ± 92.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sE-selectin</td>
<td>Before</td>
<td>5791.3 ± 2250.2</td>
<td>7.838</td>
</tr>
<tr>
<td>After</td>
<td>3027.1 ± 1640.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NB-UVB, narrow-band ultraviolet-B; sE-selectin, soluble E-selectin; sICAM-1, soluble intercellular cell adhesion molecule-1. *P value <0.05 was considered significant.

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**Figure 1**

A female patient before treatment with NB-UVB (PASI = 22). NB-UVB, narrow-band ultraviolet-B; PASI, Psoriasis Area and Severity Index.

**Figure 2**

A female patient after treatment with NB-UVB (PASI = 4). NB-UVB, narrow-band ultraviolet-B; PASI, Psoriasis Area and Severity Index.
with controls, but with no statistical significance ($P = 0.240$). This difference may be due to the fact that in their study the average age of the control group was 15 years higher than that of the patients.

With regard to the patient group, there was a statistically significant difference regarding sE-selectin serum levels before and after NB-UVB phototherapy ($P = 0.001$). These results were consistent with those of Bonifati et al. [22], Carducci et al. [23], D'Auria et al. [25], Szepietowski et al. [26], Borskà et al. [19], and Long et al. [3]. However, Krasowska et al. [27], Kowalzick et al. [21], and Czech et al. [23] did not find a significant difference in sE-selectin serum levels before and after treatment with dithranol and combined dithranol and UVB. The reasons for these conflicting study outcomes might be related to differences in the study regimens, study designs, or patient population characteristics.

Also, there was a statistically significant difference regarding sICAM-1 serum levels before and after NB-UVB phototherapy ($P = 0.001$), which is in agreement with Batycka-Baran et al. [20]. In contrast, Borskà et al. [19], Kowalzick et al. [21], and Long et al. [3] found no statistically significant difference in serum levels of sICAM-1 before and after treatment with Goekerman's therapy, topical dithranol + UVB, and NB-UVB phototherapy, respectively.

Serum levels of sE-selectin after NB-UVB phototherapy, although lower than the pretreatment level in the present study, were still higher than that found in healthy controls, as was also found by Borskà et al. [19], Long et al. [3], and Krasowska et al. [27]. The reason for the increased serum sE-selectin levels remains unknown, although it is indicative of an altered endothelial function in psoriasis.

A significant positive correlation was found between sE-selectin serum levels and PASI scores before and after NB-UVB phototherapy, which was in agreement [28], Kowalzick et al. [21], Carducci et al. [23], Bonifati et al. [22], and Krasowska et al. [27], although this finding was against Czech et al. [24] and Long et al. [3]. This may be due to the use of different method for treatment (topical steroid) [24] and different number of patients in their studies ($n = 16$ and $58$ respectively).

Significant positive correlation was found between sICAM-1 serum levels and PASI scores before and after NB-UVB. These results were in agreement with Gangemi et al. [18], Ameglio et al. [29], Borskà et al. [19], Čabrijan and Lipozenčič [5], and Long et al. [3]. On the contrary, Krasowska et al. [30] had not found any correlation between plasma levels of sICAM-1 and PASI scores.

### Conclusion

The study emphasizes the complex nature of the roles played by sCAMs in the immunopathogenesis of psoriasis and the effect of NB-UVB on their values in relation to PASI score. Also results of this study provide rationale for possible application of sE-selectin and sICAM-1 serum measurement as biomarkers of psoriasis activity. Adhesion molecules are currently considered as possible targets of future psoriasis therapies but still needs further studies.

### Acknowledgements

Conflicts of interest

None declared.

### References


7. Pober JS, Bevilacqua MP, Mendrick DL, Cotran RS, Gimbrone MA Jr, Two distinct monokines, interleukin 1 and tumor necrosis factor, each...


