Analysis of the Epidermal Shield against Broadband Ultraviolet B-Induced Erythema

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Abstract. Background. Recent accumulating data in the literature indicates a complex photoprotective role of the epidermis where the role of melanin as the major photoprotective mechanism has become debatable. Aim. To make a comparative assessment of the photoprotective roles played by different epidermal structures. Methods. 40 patients with vitiligo, with skin phototypes (SPTs) II to V, were enrolled in the study. Areas of skin (lesional and nonlesional) were delineated where the stratum corneum (SC) was stripped from half of each area to obtain 4 skin models: lesional, lesional stripped, nonlesional, and nonlesional stripped. After 24 h, skin models were exposed to broadband ultraviolet B (BB-UVB) irradiation, to measure the minimal erythema dose (MED) values which were used to indirectly assess the photoprotective role of each epidermal structure; melanin, viable epidermis (VE), and SC. Results. The MED values were significantly \( (P < 0.001) \) different among skin models for almost all comparisons, being highest in nonlesional skin, followed by nonlesional stripped, lesional, and lesional stripped skin, and a significant \( (P < 0.001) \) positive correlation was observed between MED and SPT. There were also significant \( (P < 0.001) \) differences in MED values calculated for epidermal structures for almost all comparisons, being highest for VE, followed by melanin, and then the SC, and a significant \( (P < 0.001) \) positive correlation was observed between MED and SPT. Conclusion. Epidermal photoprotection extends beyond melanin production and may involve several factors such as epidermal thickness, optical properties, and chromophores. Such a role was perceived to be reactive to ultraviolet radiation (UVR) and more efficient in those with higher SPTs.

Keywords: Photoprotection, Eidermis, Melanin, Stratum Corneum, Minimal Erythema Dose

1. Introduction

Melanin is considered the major defence mechanism of the skin against the hazardous effects of ultraviolet radiation (UVR) \([1, 2]\). However, some findings pointed at other potential epidermal photoprotective mechanisms. Patients with vitiligo, whose lesional skin (which is deficient in melanin) was exposed to UVR at the minimal erythema dose (MED), had a significant positive correlation with skin phototype (SPT) \([3]\). In addition, regardless of the SPT, the palms and soles, areas where the stratum corneum (SC) is thick, cannot develop sunburn after exposure to normal levels of UVR \([4]\). Several studies were carried out to explain such findings \([1, 3, 5–11]\).

In a previous experiment, we evaluated epidermal photoprotection using narrowband ultraviolet B (NB-UVB) to simulate the UVB portion of natural sunlight. Although BB-UVB would be a more appropriate choice, we were limited by the available hospital equipment by that time \([5]\). The current study represents a revision of that experiment using BB-UVB.
2. Methods

The study was approved by the institutional ethics committee, and informed written consent was obtained from all participants before enrolment.

The clinical part of the study was completed in the spring of 2011. The study comprised 40 vitiligo patients enrolled from the outpatient dermatology clinic at Ain Shams University Hospital (mean age 33.1±9.27 years, range 20–42; mean disease duration 5.62±4.13 years), whose disease distribution had to involve the abdomen and/or the volar surface of the forearm. Exclusion criteria were a history of UVR or keratolytic drugs within 2 months before the start of the study and extremes of age.

Clinical assessment and the Fitzpatrick self-report questionnaire [12] were used to select patients with an equal sample distribution of SPTs II, III, IV, and V to constitute 4 groups of equal number and gender distribution (mean ± SD age 28.3±4.13, 32.45±3.25, 31.37±4.48, and 29.7±5.12 years, resp.).

We followed the same method of our previous work in skin preparation and measurement of MED [5]. Accordingly, all patients underwent stripping of the SC in areas of both lesional and nonlesional skin. Stripping was restricted to the abdomen (n = 14) and the volar surface of the forearm (n = 26), which are areas usually protected from UVR. A standard stripping procedure was performed by a single investigator, where random histological testing confirmed the stripping of appropriate amount of the SC. Consequently, 4 adjacent skin models: nonlesional (N), stripped nonlesional (NS), lesional (V), and stripped lesional (VS), were developed for each patient.

Measurement of MED was not carried out until 24 h after stripping to ensure clearance of the inflammation and to precede the epidermal proliferative response. We followed our hospital phototherapy protocol to measure MED. We used 100 L UV therapy unit; Waldmann Medical Division, Schwenningen, Germany, containing 8 UV-6 100-watt lamps emitting wavelengths of 280–360 nm with the maximum at 351 nm. Each patient was exposed to a test dose ladder of BB-UVB (30 mJ/cm² initial dose and 20% increments) to test each skin model for MED. A single blinded investigator assessed erythema 24 h after UV exposure. Accordingly, MED values were determined in all SPT groups for the four skin models. (Table 1 and Figure 1).

We indirectly calculated the MED for each epidermal structure through those determined for skin models, where the SC equals “lesional minus stripped lesional” and melanin equals “nonlesional minus lesional,” while the remainder of viable epidermis (VE) was directly represented through stripped lesional model (Table 1 and Figure 1).

Data analysis was performed using the one-way ANOVA for multiple quantitative groups, t-test for paired groups, and the Spearman 𝜌-test for correlations. 𝑃 ≤ 0.05 was considered significant.

3. Results

MED values (mJ/cm²) for all groups are listed in Table 1. All groups were matched for age and gender, and there was no significant correlation between MED and either age or gender. There were significant (𝑃 < 0.05) differences in the MED values of skin models, being highest in nonlesional skin, followed by stripped nonlesional, lesional, and stripped lesional skin. Similar significance levels were seen within each SPT group for almost all comparisons. A trend towards increasing MED values was found within matched models in sequential SPTs (Figure 1), and there were significant (𝑃 < 0.001) positive correlations between SPT and MED for all skin models (stripped lesional 𝑟 = 0.976, lesional 𝑟 = 0.987, stripped nonlesional 𝑟 = 0.992, and nonlesional 𝑟 = 0.996).

<table>
<thead>
<tr>
<th>Test group</th>
<th>Skin phototype</th>
<th>II (𝑛 = 10)</th>
<th>III (𝑛 = 10)</th>
<th>IV (𝑛 = 10)</th>
<th>V (𝑛 = 10)</th>
<th>Total (𝑛 = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin models</td>
<td>VS</td>
<td>104.1±21.1</td>
<td>116.8±27.3</td>
<td>140.1±32.8</td>
<td>145.6±37.5</td>
<td>124.3±33.8</td>
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<tr>
<td></td>
<td>V</td>
<td>124.8±25.3</td>
<td>140.1±32.8</td>
<td>164.9±39.1</td>
<td>174.5±45.1</td>
<td>150.4±40.2</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>137±29.3</td>
<td>151.3±39</td>
<td>173±50.6</td>
<td>183.6±60.2</td>
<td>160.1±48</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>154.4±26.8</td>
<td>170.1±36</td>
<td>195.1±50</td>
<td>211.2±60.5</td>
<td>180.1±48.8</td>
</tr>
<tr>
<td>Epidermal structures</td>
<td>SC †</td>
<td>20.7±4.3</td>
<td>23.3±5.5</td>
<td>24.8±10.9</td>
<td>28.9±7.5</td>
<td>24±7.8</td>
</tr>
<tr>
<td></td>
<td>VE †</td>
<td>104.1±21.1</td>
<td>116.8±27.3</td>
<td>140.1±32.8</td>
<td>145.6±37.5</td>
<td>121.7±33.8</td>
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<tr>
<td></td>
<td>Melanin*</td>
<td>29.6±8.5</td>
<td>30±6.5</td>
<td>30.2±12.9</td>
<td>36.7±21</td>
<td>33.3±13.2</td>
</tr>
</tbody>
</table>

MED, minimal erythema dose; N, nonlesional; NS, nonlesional stripped; SC, stratum corneum; V, vitiliginous; VE, viable epidermis apart from melanin; VS, vitiliginous stripped. * MED value for each epidermal structure was calculated as illustrated: †V minus VS; ‡VS; *N minus V.
Figure 1: Comparisons among MED values (mean±SD) (mJ/cm\(^2\)) tested for skin models.

Figure 2: Comparisons among MED values (mean±SD) (mJ/cm\(^2\)) calculated for epidermal structures.
There were significant ($P < 0.001$) differences in MED values calculated for the epidermal structures, being highest for the SC, followed by melanin and VE. Similar significance levels were seen within each SPT group. A trend towards increasing MED values was also seen within matched epidermal structures in sequential SPTs (Figure 2), and there were significant ($P < 0.001$) positive correlations between SPT and MED calculated for the SC ($r = 0.982$), melanin ($r = 0.818$), and VE ($r = 0.976$).

4. Discussion

Our findings should be perceived in relation to the "epidermal shield against UVB-induced erythema" rather than the "cutaneous shield against UVB hazards." In this context, the epidermis, other than its melanin content, plays a complex photoprotective role, via several factors, including thickness, optical properties, and chromophore content. This photoprotection has previously been reported to correlate with SPT [3].

MED reflects the sensitivity of the skin to UVR and the value of photoprotection [13]. In our previous work [5], we have used narrowband UVB to simulate the UVB proportion of natural sunlight, the choice that was exposed to some criticism being less representative than broadband UVB. Unfortunately, we were limited to the available equipment in our hospital by that time. Currently, we carried out a similar experiment with the implication of BB-UVB to obtain more reliable data and judge our previous findings. Factors that may influence MED such as gender [14], extremes of age [15], and UV-induced epidermal hyperplasia [16] were taken into consideration. Moreover, we adopted self-control comparisons to avoid the influence of individual variation.

Results were close to our previous work and confirmed the main outcome. In different skin models, the significant positive correlation between SPTs and MED reflected the increasing UVB tolerance obtained with increasing SPT. For nonlesional skin, this was attributable to the increase in melanogenesis, which may be considered a photoprotective response to DNA damage [2, 17]. However, the same correlation was seen in lesional skin, which is deficient in melanin, and this indicates that there are photoprotective mechanisms other than melanin, which are also photoreactive and increase in line with the SPT, a finding that agrees with previous reports [3, 6].

As expected, there was a significant decrease in MED for lesional compared with nonlesional skin, either stripped or not, and this was attributable to the known photoprotective effect of melanin [1]. However, there was also a significant decrease in MED between stripped and unstripped skin models, indicating the photoprotective value of the SC. This may be explained by the thickness of this layer [6], its ability to reflect 5–10% of incident light [11], and its urocanic acid (UCA) content [18]. Epidermal UCA is relatively concentrated in the SC and is mainly involved in UV-induced immunosuppression; its role in photoprotection is still debatable [8, 19].

In 1996, Gniadecka et al. reported the main contributors to epidermal photoprotection to be the SC and melanin; in neither vitiliginous nor normally pigmented skin did the photoprotection depend on VE [6]. However, a controversy over their methodology and quality of data arose two years later [8]. In 2002, the role of VE in epidermal photoprotection was reported by other authors, but melanin was still considered more important [10]. In the current study, a significant increase in MED was found for VE compared with other epidermal structures in the vitiligo group and within the various SPT groups, a finding that seems to indicate an important role for the VE in photoprotection. This may be due to its thickness [10], content of chromophores such as UCA [18], and content of proteins, aromatic amino acids [7], and DNA, where the cellular nature of the VE ensures its significance [11]. Abstractly, VE represents part of epidermal shield against UVR-induced dermal responses but, actually, the potential risk of skin cancer through UVR-induced DNA damage introduces it (with its high DNA content) as an exposed rather than photoprotective structure.

There is no question that the photoprotective value of melanin is greater than that of the SC, the finding which was evident within almost all groups. It was previously reported that the SC may be the main photoprotective factor not only in vitiliginous skin but also in normally pigmented skin [6]. In this study, we confirmed the value of the SC rather than its relative priority compared with melanin.

The significant positive correlations we found between the SPTs and MED for melanin, the SC, and the VE reflected an increasing tolerance to UVB with higher SPT. It is already known that melanin content increases with higher SPT values [2, 17]. Taking into consideration that skin thickness does not change with SPT [20], the increasing tolerance to UVB for either the VE or the SC may be attributable to other epidermal photoprotective factors that increase with increasing SPT.

5. Conclusion

We conclude that epidermal mechanisms other than melanin may play a role in photoprotection, and that these mechanisms are photoreactive and increase with increasing SPT. Several mechanisms may be at work, including epidermal layer thickness, optical properties, and chromophore content. Further studies may clarify the specific photoprotective mechanism of each of these mechanisms and thus provide new perspectives on cutaneous photoprotection.

References


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I am pleased to share with you that Nuclear Receptor Research is now a reality as an open access peer-reviewed journal devoted to publishing high-quality, original research and review articles covering all aspects of basic and clinical investigations involving members of the nuclear receptor superfamily. Nuclear Receptor Research has an editorial board comprised of a group of renowned scientists from around the world. Board members are committed to make Nuclear Receptor Research a vibrant forum showcasing global efforts in this ever-expanding area of research.

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Editor-in-Chief
Nuclear Receptor Research