Synergistic Effect of Broad-Spectrum Sunscreens and Antihistamines in the Control of Idiopathic Solar Urticaria

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Background: It can be difficult to provide patients with idiopathic solar urticaria adequate protection from sunlight. In a nonrandomized controlled trial, we used a standardized phototest procedure to determine the effects of using sunscreen and antihistamine to control idiopathic solar urticaria.

Observations: Three patients with idiopathic solar urticaria underwent phototesting with UV-B and UV-A radiation. The minimal urticarial dose (MUD) was determined 15 minutes after irradiation. The patients were subsequently tested with 5 times the MUD, and the reaction was graded every minute for 15 minutes. The patients were then treated with a high-protection, broad-spectrum sunscreen and a nonsedative antihistamine alone and in combination and underwent similar phototesting. The use of sunscreen allowed the patients to tolerate much higher doses of UV radiation (32-38 times the MUD on untreated skin). Antihistamine use did not increase the patients’ MUD but did suppress wheal formation and itch, and only immediate erythema sharply localized in the irradiated areas occurred. The combination of sunscreen and antihistamine acted synergistically and increased the tolerance to UV radiation markedly (80-267 times the MUD on untreated skin).

Conclusion: High-protection, broad-spectrum sunscreens and antihistamines protect patients with solar urticaria in different ways and are highly effective when combined.

Arch Dermatol. 2008;144(6):765-769
developed for the phototest procedure to determine the beneficial effect of combined sunscreen and antihistamine use. In the present study, we address this issue.

**METHODS**

**PATIENTS**

Three patients (1 man and 2 women; age range, 33-63 years) diagnosed as having idiopathic solar urticaria in the past year underwent phototesting. The diagnosis was confirmed by means of provocation testing with UV-B, UV-A, and blue light, with development of a clearly visible itchy erythema and wheal formation during or shortly after irradiation. Other photosensitivity diseases were ruled out by screening for antinuclear antibodies and plasma porphyrins and by performing a 5-day provocation test for polymorphic light eruption. None of the patients were taking any photosensitizing medications. Two patients reacted to UV-B and UV-A, and 1 patient was sensitive to UV-A and blue light.

**RADIATION SOURCE AND PROCEDURE**

The UV sources were a bank of Philips TL12 tubes emitting broad-band UV-B and a bank of Philips TL10 tubes producing UV-A (Philips, Eindhoven, the Netherlands). Irradiance was measured using a UV spectroradiometer (Sola-Hazard; Solatell, Cornwall, England). The calibration of this equipment is traceable to the National Physical Laboratory of the United Kingdom. All UV doses were quantified using the standard erythema dose (SED) (10 mJ/cm² at 298 nm using the Commission Internationale de L'Eclairage [International Commission on Illumination] erythema action spectrum).8

Irradiation was conducted by placing a MED Test Patch (Chromo-Light, Copenhagen) directly on the skin; 6 windows of 1.2 cm each allowed UV radiation to pass through with a dose increment of 25% (Figure 1A). A test of the transmission in the windows was performed using a light measurement system (IL1700) with a detector (SED 240) (International Light, Newburyport, Massachusetts). The urticarial reaction in response to UV irradiation was initially confirmed (Figure 1B).

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**Figure 1.** Minimal urticarial dose (MUD) test results. A, The test patch used in the phototest procedure. B, The urticarial response in 1 patient after exposure to UV-B (0.1 standard erythema dose [SED]). C, The MUD determination with UV-B (0.05 SED). The MUD was determined in the area with just-perceptible immediate erythema. Erythema that spreads beyond the borders of 1 of the areas irradiated with a higher UV dose than the MUD illustrates a ++ reaction (ie, erythema spreading beyond the irradiated area). D, The urticarial reaction with sunscreen after exposure to UV-B (2.0 SED). E, The urticarial reaction after antihistamine treatment and irradiation with UV-B (0.1 SED).
At a given wavelength, the minimal urticarial dose (MUD) is defined as the dose that induces a clearly visible itching erythema or whealing during or shortly after irradiation. The UV dose needed to induce just-perceptible erythema (the MUD) was determined 15 minutes after irradiation because preliminary experiments had shown that this period allowed for the reaction to develop and reach a maximum. Subsequently, the patients were tested with 5 times the MUD, and the reactions in the various areas were graded every minute for 15 minutes starting immediately after irradiation to follow the development of the reaction. Irradiance with UV-B lasted seconds to a few minutes, but irradiance with UV-A was longer (minutes to hours) and was, therefore, not possible in all experiments.

The induced reaction was graded visually according to an established 6-point scale: 0 indicates no reaction; (+), just-perceptible erythema (MUD) (Figure 1C); +, erythema localized to the irradiated area; ++, erythema spreading beyond the irradiated area; ++++, wheals in some parts of the irradiated area; and +++++, wheals in the entire irradiated area.

**SUNSCREEN AND ANTIHISTAMINE TREATMENT**

After determination of the MUD on irradiated but untreated skin, a sunscreen (sun protection factor [SPF] of 60/immediate pigment darkening of 16; absorption spectrum, 200-400 nm) (Vichy 60/16; Vichy Laboratories, Paris, France), 2 mg/cm², containing the filters titanium dioxide, octocrylene, butyl methoxydibenzoylmethane, and terephthalylidene dicamphor sulfonic acid was applied 20 minutes before irradiation and was left on the skin for 15 minutes. Antihistamine treatment consists of fexofenadine hydrochloride (Telfast; Sanofi-Aventis, Paris) with a half-life of 14 hours was administered orally 1 hour before irradiation at a dose of 360 mg, and the patients were tested again with and without application of sunscreen.

The doses needed to produce just-perceptible erythema (the MUD) and wheal formation when exposed to UV-B and UV-A are given in Table 1 and Table 2, respectively. The use of sunscreen with a high protection factor (SPF 60/16) provided marked protection in the patients and allowed for the use of much higher doses of UV radiation before urticaria formation (32-36 and 38 times the MUD on untreated skin for UV-A and UV-B, respectively) (Figure 1D). The stated SPF did not relate to the urticarial protection achieved.

On the contrary, the use of antihistamines did not increase the MUD but did suppress the urticarial reaction markedly. As visualized in Figure 1E, it was not possible for us to make the reaction develop into more than a + reaction with the UV doses used. Thus, the erythema stayed localized to the irradiated areas, with no wheal formation (Figure 2). In the combined sunscreen and antihistamine experiments, the erythema did, however, spread a bit beyond these borders after the high doses of UV-B used in this testing (80 times the MUD on untreated skin). After antihistamine treatment, the patients had no itching.

The combination of sunscreen and antihistamine was especially effective because it increased the tolerance to UV radiation markedly before urticaria formation (80-267 times the MUD on untreated skin) and suppressed the urticarial reaction, keeping it from developing into a wheal. The effect was synergistic compared with the separate treatments (Table 1). The UV-A testing of the combination of sunscreen and antihistamine was not pos-

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**Table 1. Dose of UV-B and UV-A Needed to Provoke Just-Perceptible Immediate Erythema**

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>No Treatment</th>
<th>Sunscreen</th>
<th>Antihistamine</th>
<th>Sunscreen Plus Antihistamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV-B, SED (MUD)</td>
<td>1/M</td>
<td>0.040</td>
<td>1.5 (×38)</td>
<td>0.040 (×1)</td>
</tr>
<tr>
<td></td>
<td>2/F</td>
<td>0.064</td>
<td>2.4 (×38)</td>
<td>0.083 (×1.5)</td>
</tr>
<tr>
<td>UV-A, SED (MUD)</td>
<td>1/M</td>
<td>0.006</td>
<td>0.2 (×33)</td>
<td>0.006 (×1)</td>
</tr>
<tr>
<td></td>
<td>2/F</td>
<td>0.007</td>
<td>0.2 (×32)</td>
<td>0.008 (×1)</td>
</tr>
<tr>
<td></td>
<td>3/F</td>
<td>0.066</td>
<td>2.4 (×36)</td>
<td>0.086 (×1)</td>
</tr>
</tbody>
</table>

Abbreviations: MUD, minimal urticarial dose; NA, not applicable; SED, standard erythema dose.

a Patient 3 did not react to UV-B. The times of irradiation for the UV-A testing of sunscreen combined with antihistamine were too long to be practical.

**Table 2. Dose of UV-B and UV-A Needed for Wheal Formation**

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>No Treatment</th>
<th>Sunscreen</th>
<th>Antihistamine</th>
<th>Sunscreen Plus Antihistamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>UV-B, SED (MUD)</td>
<td>1/M</td>
<td>0.06</td>
<td>1.5 (×41)</td>
<td>&gt;0.20 (×4)</td>
</tr>
<tr>
<td></td>
<td>2/F</td>
<td>0.12</td>
<td>7.5 (×60)</td>
<td>&gt;1.00 (×8)</td>
</tr>
<tr>
<td>UV-A, SED (MUD)</td>
<td>1/M</td>
<td>0.01</td>
<td>0.6 (×64)</td>
<td>&gt;0.03 (×3)</td>
</tr>
<tr>
<td></td>
<td>2/F</td>
<td>0.01</td>
<td>0.7 (×70)</td>
<td>&gt;0.04 (×4)</td>
</tr>
<tr>
<td></td>
<td>3/F</td>
<td>0.10</td>
<td>&gt;2.4 (×24)</td>
<td>&gt;0.30 (×3)</td>
</tr>
</tbody>
</table>

Abbreviations: See Table 1.

a In some testing experiments, it was not possible to provoke a wheal reaction with the UV doses used (indicated by the “*” sign) (ie, the tolerance is more than the dose given). 

b Patient 3 did not react to UV-B. The times of irradiation for the UV-A testing of sunscreen combined with antihistamine were too long to be practical.
Idiopathic solar urticaria is a rare but, in some cases, severely incapacitating disease. Patients are extremely sensitive to UV radiation, most commonly UV-A, visible light, and infrared light. On sun exposure, patients develop erythema, itching, and whealing, and with total body exposure, they may develop anaphylaxis. In some patients, tolerance to sunlight is so low that they cannot stay in the sun more than a few seconds before reacting. The disease may, therefore, affect the lives of the patients tremendously.

In this study, we developed a novel standardized method to determine the MUD in patients with solar urticaria. At a given wavelength, the MUD has previously been defined as the dose that induces clearly visible itchy erythema or whealing during or shortly after irradiation. In the present study, all the patients developed immediate itchy erythema within a few seconds or minutes when exposed to causal wavelengths of UV radiation and immediate wheal formation in areas with higher UV doses, which is characteristic of patients with solar urticaria. The MUD was determined 15 minutes after exposure to UV radiation because the skin reaction was stable at this time point. In addition to the MUD, the time course for the various reaction steps was determined by grading the reaction every minute after UV irradiation.

Moreover, we tested the effect of commonly used treatment modalities, such as sunscreen and antihistamine, in preventing idiopathic solar urticaria. We showed that the use of a broad-spectrum sunscreen with a high SPF (Vichy 60/16) applied in the recommended amount of 2 mg/cm² allowed much higher UV doses before urticaria development (32-38 times the MUD on untreated skin). In contrast, the use of an antihistamine did not increase the MUD of the patients but did suppress the urticaria symptoms. With the doses used, we were thus able to provoke only immediate erythema with sharp demarcation but not wheal formation or itch. The combination of sunscreen and antihistamine acted synergistically, resulting in the need for high doses of UV before urticaria formation (80-267 times the MUD on untreated skin) and suppression of the urticarial reaction. The degree of protection using the different treatments was similar for all the patients (Table 1). This is interesting because previous studies report a highly variable effect of antihistamines and sunscreens in patients.

A few earlier studies have addressed solar urticaria and possible methods of suppression. It has been described that the use of antihistamines does not increase the threshold dose for erythema localized to the irradiation site but does increase the threshold for wheal development, which the present findings confirm. The effect of sunscreens has not been elucidated more thoroughly either alone or combined with an antihistamine.

The present findings indicate that when the 2 most sensitive patients in this study are protected properly using a high-protection broad-spectrum sunscreen and an antihistamine, they may stay in the Danish summer sun (6 SED per hour) for 30 minutes to 1 hour before the development of symptoms compared with only a few seconds without protection. The third patient reacted to UV-A only, and it was not practical to test the combination of antihistamine and sunscreen. Yet, the use of sunscreen alone increased his tolerance to UV-A from a few minutes to more than an hour. This is a marked difference and may increase patients’ quality of life immensely because they are not confined to their houses in the daytime. The emission spectrum of the light sources used was not similar to the solar spectrum. If patients are sensitive to visible light, their protection will be less because sunscreens do not block these wavelengths. However, greater protection from UV radiation can be expected in the morning or the afternoon, when the shorter wavelengths are decreased.

In conclusion, this study shows that antihistamines and sunscreens protect patients with solar urticaria in diff-

Figure 2. Time course of the urticarial reaction for 1 patient after provocation with 5 (A) or 2.5 (B) minimal urticarial doses (MUDs) of UV-B. For each treatment, the MUD was determined and was increased when sunscreen was used. Therefore, the MUDs shown in the figure differ. The time course is representative of both patients sensitive to UV-B. Phototesting with UV-A shows a similar picture. The “Radiation Source and Procedure” subsection of the Methods section provides an explanation of the erythema reaction scale. The sunscreen used had a sun protection factor of 60/immEDIATE erythema or whealing during or shortly after irradiation.
fferent ways and are effective when combined. This finding stresses the need for careful instruction of patients in the use of antihistamines and sunscreens applied in the recommended manner and amount.

Accepted for Publication: August 16, 2007.
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Author Contributions: All the authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Faurschou and Wulf. Acquisition of data: Faurschou and Wulf. Analysis and interpretation of data: Faurschou and Wulf. Drafting of the manuscript: Faurschou. Critical revision of the manuscript for important intellectual content: Faurschou and Wulf. Statistical analysis: Faurschou. Administrative, technical, or material support: Wulf. Study supervision: Wulf.

Financial Disclosure: None reported.

REFERENCES


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