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Topical Salicylic Acid Interferes with UVB Therapy for Psoriasis

B. KRISTENSEN and O. KRISTENSEN

Department of Dermatology, Central Hospital, Karlstad, Sweden

Salicylic acid has been widely used in the topical treatment of psoriasis. Chemically it is closely related to paraaminobenzoic acid. Following in vitro studies indicating that salicylic acid might exhibit relevant UVB absorption, we found that salicylic acid had a clinically pronounced filter effect when applied prior to UVB exposure. The duration of photoprotection after application was more than 12 h, sometimes exceeding 24 h. In a prospective, randomized, double-blind, left-right comparison study in patients with psoriasis between emollients with and without salicylic acid, salicylic acid was shown to decrease the clearing rate significantly. *Key words: Emollients; Light absorption; Sunscreen.*

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B. Kristensen, Department of Dermatology, Uddevalla Sjukhus, S-451 80 Uddevalla, Sweden.

UVB treatment for psoriasis has been found to be an effective treatment modality well documented by several authors (1, 2, 3). Currently UVB therapy is increasingly used especially in out-patients treated at day care centers and it is now a well established part of the therapeutic armamentarium against psoriasis. There is experimental and clinical evidence that the use of lubricants applied prior to UVB treatment enhances the penetration of light into the psoriatic plaques (4, 5, 6). As emollients have little or no influence on UV absorption in normal skin (7), the net result is an improved therapeutic index beneficial to the patient. Salicylic acid (SA) is often used before or concurrently with other topical or UVB treatments to facilitate their access to the underlying psoriatic lesions. The molecular formula of SA (2-hydroxybenzoic acid) is structurally closely related to that of paraaminobenzoic acid (PABA), a classic photoprotective agent. Although SA was estimated long ago to have 60% of the photoprotective efficacy of PABA (8), this characteristic seems to have been forgotten or less appreciated in the context of modern phototherapy.

In the past we have routinely used emollients with SA added prior to UVB therapy in order to gain the additional benefit of a descaling component. From our observations and experience at our out-patient center, where close to 20 000 light treatments a year are given, we had reason to believe that SA could act as a UV absorber of a magnitude that could be of clinical relevance (9).

The objective of the current study has been twofold: 1) To detect any difference in clearing rate of clinical interest between emollients commonly used in conjunction with UVB treatment for psoriasis; and 2) To delineate the theoretical background for the above observation on SA and to evaluate its possible clinical implications. To our knowledge no such study has previously been published.

MATERIAL AND METHODS

In vitro study

Different emollients (Cremor Essex, Cremor Pharmacia, Cremor Locobase, Cremor Decubal, Unguentum Merck and white petrolatum), and a non-light-absorbing cream (Cremor Essex) with 2% SA were studied with regard to their photoabsorbing qualities within the wavelengths 200–400 nm. The equipment used was a Zeiss Spektral photometer D M 4 equipped with double-beam halogen and deuterium lamps and scanning with a spectral bandwidth of 2 nm. The emollients were dissolved in either isopropanol, chloroform or both. The solvents were used as controls. For comparative reasons spectral absorption curves for equimolar concentrations of PABA and SA dissolved in ethanol were studied.

In vivo studies

Clinical phototesting was performed in five volunteers with 2 Philips TL 40 W/12 (UVB) lamps. Emission spectrum is seen in Fig. 1. The test subjects' minimal erythema doses (MED) were determined and in the subsequent studies multiples of MED were applied.

In the two following test series SA in the non-UVB-absorbing Cremor Essex was applied with the vehicle serving as control. The erythema was graded on a 0–4 scale. Zero denoted no erythema, 1 minimal perceptible erythema, 2 light pink erythema, 3 marked erythema, red in colour, but no oedema and 4 fiery red erythema with oedema and tenderness. The readings were taken 24 h after UVB exposure.

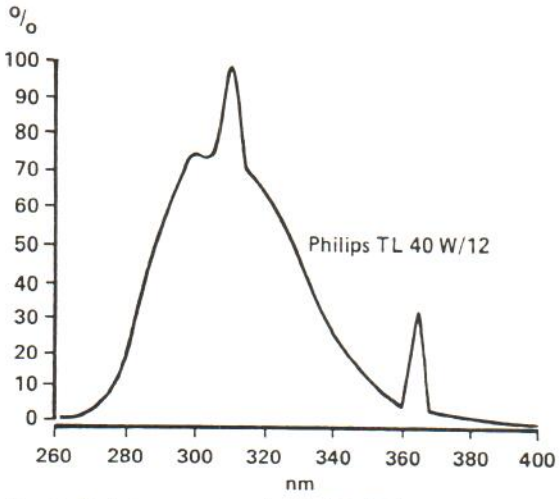

Fig. 1. Emission spectrum for the TL 12 lamp.

In the first test series we evaluated and compared the photoprotective values of different concentrations (0.5, 1, 2, 5 and 10%) of SA applied prior to as compared to after UVB exposure. In the second series the duration of the photoprotection afforded by SA was studied by applying test preparations of SA (2, 5 and 10%) at different times (1, 2, 4, 8, 12, 16, 20 and 24 h) prior to phototesting.

Clinical study

Thirty-eight consecutive patients (12 females and 26 males, mean age 45, range 20–74 years) with chronic stable plaque-type psoriasis covering > 10% of the skin and with skin types II–IV were included in the study. Twenty-nine patients completed the study. Nine patients dropped out for various reasons unrelated to the study. Systemic therapy was not allowed within 4 weeks and topical therapy within 2 weeks of entry into the study.

The prospective investigation was conducted in a randomized, half-sided, right-left double-blind fashion comparing in a single patient 2 out of 6 different preparations (5 emollients with negligible UVB photoabsorption: Cremor Essex, Cremor Pharmacia, Cremor Locobase, Cremor Decubal, Unguentum Merck) and one emollient (Cremor Essex) with 2% SA added. The emollients were applied by trained nurses at our day care center minutes prior to UVB exposure. The UVB cabins were equipped with 16 Philips TL 12 lamps giving an output of 1.35 mW/cm^2. Treatments were given 3–5 times weekly until clearance or for a maximum of 6 weeks.

The irradiation doses were increased according to the response and tolerance of the individual patient, i.e. increased at every treatment session until a slight erythema developed on either side of the body. Irradiation time was limited to a maximum of 15 min, equivalent to 1.215 J/cm^2.

Evaluation

Patients were evaluated before the start of therapy and every other week. A scoring system awarding different scores for erythema, scaling and infiltration was used. Zero denoted no symptom, 1 slight, 2 moderate and 3 severe symptoms. The different symptoms were compared for each treatment side separately. A total assessment was made adding together the scoring of the different objective symptoms.

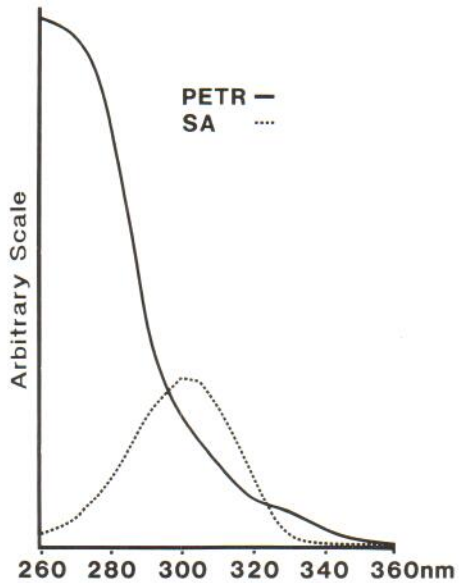

Fig. 2. Absorption spectra for Cremor Essex with 2% salicylic acid and white petrolatum.

RESULTS

In vitro study

The results of the spectral photoabsorption studies on the various emollients showed rather low and insignificant absorption within the UVB spectrum for all compounds apart from white petrolatum and 2% SA in Cremor Essex. The base Cremor Essex showed no absorption by itself. The absorption spectra for Cremor Essex with 2% SA and petrolatum are shown in Fig. 2. In the interval 295–323 nm, SA in Cremor Essex had a more pronounced absorption than white petrolatum. Below 295 nm and increasingly towards and into the UVC region, petrolatum has significant absorption that rises to high values down through the lower wavelengths.

The curves for photoabsorption by SA and a well-known photoabsorber, PABA, in equimolar concentrations (36 µmol/l) are shown in Fig. 3. As expected PABA is a much more efficient UVB filter on the whole, with a maximum peak around 285 nm. SA peaks around 303 nm and has a smaller absorption, but around 310–320 nm the two curves approach

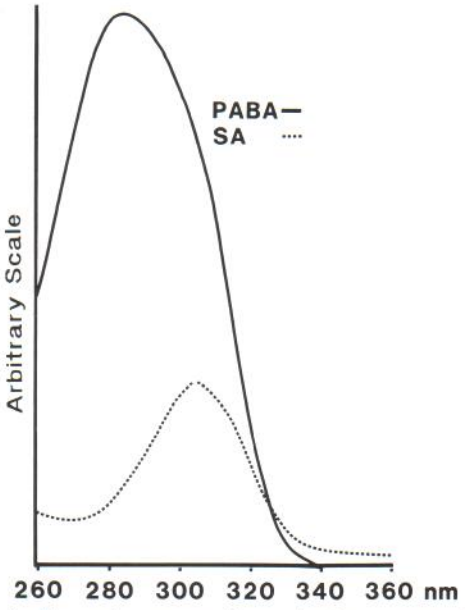

Fig. 3. Absorption spectra for equimolar concentrations (36 μmol/l) of salicylic acid and paraaminobenzoic acid.

each other, indicating that at these particular wavelengths the two chemicals are almost equal light absorbers.

In vivo studies

An example of the results using different concentrations of SA applied before and after UVB exposure is shown in Fig. 4. It was found that SA in the concentrations studied (0.5, 1, 2, 5 and 10%) had a dose-dependent inhibiting influence on UV erythema when applied prior to light exposure. When applied immediately after UV testing, no effect on erythema could be detected with any of the concentrations as compared to the cream base.

In the investigation of the duration of photoprotection given by SA, we found that it notably inhibited erythema at all concentrations (2, 5, 10%) for at least 12 h and sometimes more than 24 h.

Clinical study

The average total scores for erythema, scaling and infiltration are shown in Fig 5. Eleven patients applied an emollient containing SA on one side and an emollient without SA on the other side. Eight of these eleven patients (73%) cleared less on the side treated with the SA preparation. Three patients showed no difference. The results were statistically significant ($p < 0.01$). In patients applying different emollients without SA no statistical difference was observed.

DISCUSSION

SA is an old, but still important, keratolytic agent in the treatment of psoriasis. Whatever type of topical therapy is employed by psoriatic patients, it is important to remove scales. This also applies to UVB treatment, where it is increasingly acknowledged that lubricants applied prior to irradiation improve the optics of psoriatic skin, allowing more light energy to be absorbed in the lesions.

There are many different creams and ointments to choose from when selecting an emollient. We were interested in ascertaining if there would be any noticeable differences among the emollients we commonly use in conjunction with UVB therapy. This treatment modality is enjoying growing popularity and substantial numbers of psoriasis patients are now treated with phototherapy. To our knowledge many also use SA when undergoing UVB therapy.

By investigating the spectral photoabsorption of the different emollients, we found that only petrolatum and SA showed some absorption in the UVB range 300–320 nm known to clear psoriasis. SA was the more efficient of the two.

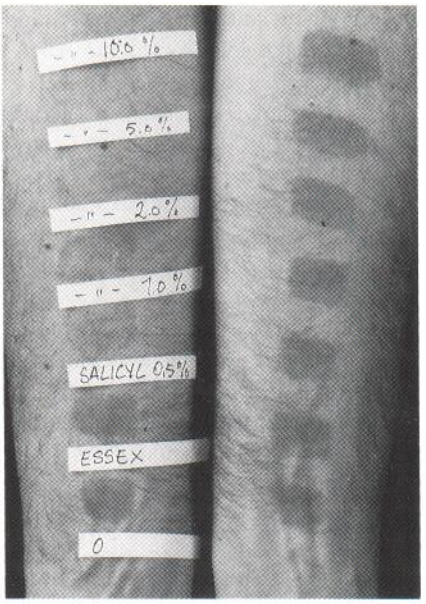

Fig. 4. Results of phototesting with different concentrations (0, 0.5, 1, 2, 5 and 10%) of salicylic acid applied on one arm prior to as compared to after irradiation on the other.

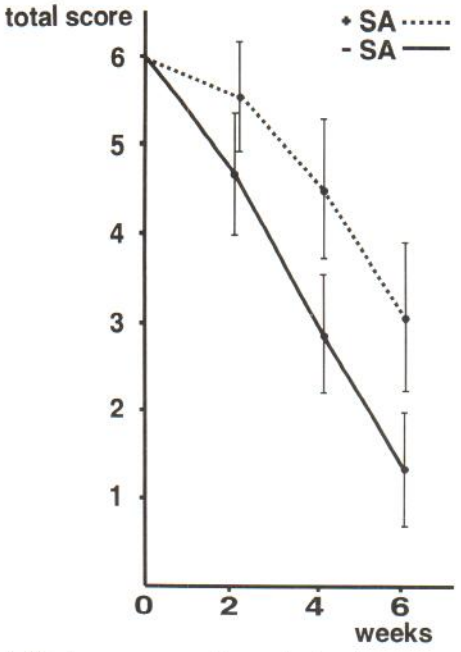

Fig. 5. Total average scores for psoriasis patients treated with UVB / emollients with as compared to without salicylic acid. Means ± SEM.

In order to estimate the magnitude of photoprotection rendered by SA, we chose to compare it with the chemically closely related PABA, a standard UVB filter. As anticipated, PABA was found to be many times more effective when the whole UVB spectrum was considered, but around 313 nm, the wavelength at which psoriasis healing is estimated to reach its optimum (10), the absorption curves of the two agents approximated to show less difference.

To evaluate the possible clinical implications of SA/UVB, we first conducted phototoxicity studies on humans with different clinically relevant concentrations of SA. We could verify a dose-dependent photoprotection when SA was applied before UVB. As the UVB erythema is known to be prostaglandin-mediated, the inhibiting effect of SA might theoretically have been of antiinflammatory nature. However, this idea could be discounted, as SA applied after UVB stimulation had no discernible influence on the erythema. This is consistent with the results of a recent study on acetylsalicylic acid by Väänänen & Hannuksela (11). The recorded UVB-protective properties of SA might also have been of short duration and thus possibly of less clinical interest. Studying the duration of protection, however, we found it to be more than 12 h and sometimes more than 24 h. After these basic investigations, we performed a double-blind clinical trial on patients with plaque psoriasis. Most subjects (73%) were found to clear less or more slowly on the side pretreated with SA.

We have come to the conclusion from this study that SA provides photoprotection of sufficient degree and duration to warrant advising our patients not to use SA concomitantly with UVB therapy.

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