

R.M. Guinovart*, J.M. Carrascosa y C. Ferrándiz

Departamento de Dermatología, Hospital Universitario Germans Trias i Pujol, Badalona, España

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*Autor para correspondencia.

Correo electrónico: rosa_guinovart@hotmail.com
(R.M. Guinovart).

Randomized Double-blind Comparative Study of 8-Methoxypsoralen Bath Plus UV-A Treatment Regimens

Estudio comparativo randomizado a doble ciego de regímenes de tratamiento con 8-metoxypsoraleno en baño-PUVA

To the editor:

Psoralen-UV-A (PUVA) therapy with topical 8-methoxypsoralen (8-MOP) is a widely used treatment for patients with moderate to severe psoriasis.^{1,2} The current regimen for bath PUVA involves soaks in a diluted 8-MOP bath followed by UV-A irradiation twice weekly. Bath PUVA has several advantages over oral PUVA as it avoids the adverse effects of oral psoralen administration (gastrointestinal disturbances and the need to use protective eyewear for 24 h after ingestion), produces a more direct psoralen bioavailability to the skin, and requires lower doses of UV-A, resulting in shorter treatment times.

Previous studies investigating the characteristics of PUVA erythema found peak erythematous responses at 96 to 120 h.³⁻⁵ In addition, we have previously shown that skin remains significantly photosensitive for up to 2 days following trimethylpsoralen (TMP) bath PUVA, possibly due to the presence of psoralen-DNA monoadducts. These findings suggest that in order to achieve the same therapeutic response it may not be necessary to repeat photosensitization prior to the second weekly exposure to UV-A. We have examined this hypothesis.

Approval for the study was obtained from the Tayside Research Ethics Committee, Dundee, Scotland. Patients with symmetrically localized plaque psoriasis on the limbs who were referred for bath PUVA were invited to participate in the study; all participants signed a written informed consent form. The subjects recruited had a minimal phototoxic dose assessment performed by UV-A irradiation immediately after a 15-min soak in 8-MOP solution (3 mL of 1.2% 8-MOP solution [Crawfords Pharmaceuticals, Milton Keynes, United Kingdom] in 15 L of water). The minimal phototoxic dose was determined at 72 h.

Patients were randomized to receive 8-MOP soaks twice weekly followed by UV-A irradiation on 1 limb or an 8-MOP soak 1 day of the week and placebo at the time of the second treatment, followed by UV-A irradiation on the other limb.

The random allocation list was generated by computer and allocations were concealed in sequentially numbered opaque envelopes containing the words active (twice-weekly soaks) or

inactive (once-weekly soak). Randomization was controlled by the research nurse and carried out after patients had given their written consent to participate in the study.

Sixteen patients (9 women and 7 men) with symmetrically localized plaque psoriasis on the arms or legs participated in the study. Patients less than 18 years of age, on photoactive medication, and those who had received systemic treatment for psoriasis or phototherapy, photochemotherapy, or sunbed therapy in the preceding 3 months were excluded from the study. The treatment was limited to the arms or legs. The majority of patients underwent treatment of the arms (13 patients) and in the remaining 3 patients the treatment was applied to the legs.

During the study, topical steroids and antibiotic or antimycotic preparations were allowed for application only to the flexures and scalp; only emollients were permitted elsewhere. Treatment was performed in accordance with the protocol for stepped incremental UV-A therapy established in this unit. If a patient missed a treatment, the next soak administered was the active soak. Treatment was discontinued at clearance or with 4 exposures after achieving minimal residual activity. The data gathered included total number of treatments and total dose of UV-A to clearance or minimal residual activity, time to relapse, and psoriasis severity score in the plaques.

Patients were followed up at 2, 4, and 6 months and at 1 year.

The scaling, erythema, and induration (SEI) score was recorded for selected plaques at each visit. The nurses who administered the soaks, the patients, and the clinician scoring the plaques were blinded to the treatment allocation. In order to determine psoriasis severity on the study limbs over the course of study, we analyzed the area under the curve of SEI scores over time in all patients. There was a seemingly greater reduction in psoriasis severity on the limbs that received two 8-MOP soaks per week, although the difference between the 2 sides did not reach statistical significance in this small study ($P=0.29$, Wilcoxon signed rank sum test).

Among the 6 patients who attended follow-up, only one showed a difference in time to relapse on the 2 treated limbs; relapse occurred 2 months later on the 'active' (twice-weekly soak) limb.

The aim of this double-blind, intrasubject comparative study was to determine whether omitting one of the 8-MOP baths each week reduced the risk of burning without loss of therapeutic efficacy. A number of difficulties were encountered during the course of the study: patient recruitment was limited by the fact that patients with localized psoriasis are usually managed in the community with topical therapies and, if their psoriasis was generalized, only emollients were permitted; and many patients were lost to follow-up.

Despite prolonged photosensitivity with TMP-bath PUVA and 8-MOP bath PUVA, our impression from this study is that the second soak is probably important, though the size of the study did not allow us to reach a definitive conclusion.

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L. Berroeta*, I. Man, R.S. Dawe, J. Ferguson and S.H. Ibbotson

Photobiology Unit, Department of Dermatology, Ninewells Hospital and Medical School, United Kingdom

*Autor para correspondencia.

E-mail address: lauraberroeta@hotmail.com (L. Berroeta).

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Artritis reactiva por *Chlamydia trachomatis*: importancia del rastreo y tratamiento de la pareja

Reactive Arthritis Associated with *Chlamydia trachomatis* Infection: Importance of Screening and Treating the Partner

Sr. Director:

La artritis reactiva, también conocida como síndrome de Reiter, es una espondiloartropatía seronegativa que clásicamente se define por la tríada artritis, uretritis y conjuntivitis. Es secundaria a una infección gastrointestinal o genitourinaria^{1,2}.

Las manifestaciones cutáneas que se observan con mayor frecuencia son la balanitis circinada, queratodermia blenorragica y la distrofia ungueal, pero existe diversidad en los síntomas presentados y en la secuencia temporal de estos.

Describimos el caso clínico de un paciente de 23 años de edad, ingresado por sacroileitis y lesiones psoriasiformes en las extremidades y tronco, en el que también se destacaba balanitis circinada, distrofia ungueal, dactilitis, queratodermia blenorragica (fig. 1) astenia y conjuntivitis bilateral. El paciente refería episodios anteriores de artritis, conjuntivitis y uretritis, que ocurrían con un tiempo medio de incubación de 3 semanas, posterior a los síntomas de uretritis y que cedían tras la administración de antiinflamatorios no esteroideos y doxiciclina.

Durante el ingreso, el estudio analítico, presentaba como hallazgos de interés, elevación de la proteína C reactiva. El factor reumatoide no estaba elevado, el estudio de la autoinmunidad, las serologías virales y los cultivos microbiológicos para los microorganismos relacionados con las enfermedades de transmisión sexual fueron negativos. La

biopsia cutánea fue compatible con psoriasis, los antígenos de histocompatibilidad HLA-B27 fue positivo y los estudios radiográficos revelaban signos incipientes de entesitis y sacroileitis asimétrica. La pareja no presentaba sintomatología genitourinaria.

Se recogió una muestra de exudado uretral y cervical del paciente y de la pareja, para la detección de *Chlamydia trachomatis* por la reacción en cadena de la polimerasa,



Figura 1 Queratodermia blenorragica en el pie derecho.