Acta Dermatovener (Stockholm) 53: 469–472, 1973

PSORIASIS IMPROVED BY PSORALEN PLUS BLACK LIGHT

Joseph F. Walter and John J. Voorhees

From the Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan, USA

Abstract. Previous studies have shown that psoralen plus black light inhibits DNA synthesis in mammalian epidermis. This finding suggested that psoralen plus black light might be capable of suppressing the rapidly proliferating epithelium in psoriasis. The objective of this pilot clinical experiment was to answer the question as to whether psoralen plus black light could improve a psoriatic lesion. We found improvement, measured by decreased thickness and scaling of chronic plaque-type lesions, in 8 of 11 patients, with complete clearing in 2 of these 8 patients. Control sites subjected to exposure to black light or psoralen alone showed no visible change. In our view this data suggests that a psoralen + black light treatment regimen for psoriasis may be useful.

Because of the rapid epidermal proliferation in psoriasis (11), various cell cycle inhibiting agents such as methotrexate (7), hydroxyurea (4), mechlorethamine (5) and fluorouracil (9) have been used either systemically or topically and appear to inhibit cellular reproduction, thereby improving the lesions. However, the occurrence of systemic toxicity, cutaneous sensitivity, and ulceration, has been a drawback to the use of these drugs.

Epstein & Fukuyama (3), Baden et al. (2), as well as our own studies (10) have shown that psoralen plus black light inhibits the S phase (scheduled DNA synthesis) of the cell cycle. This suggested to us a possible new clinical use of psoralens and prompted the present study in which 8 of 11 psoriatics were improved by psoralen plus black light. Our pilot study confirms the preliminary report of Tronnier & Schüle (8) who, by using methodology similar to that described below, found improvement in 9 psoriatic patients.

PATIENTS AND METHODS

Patients. 11 psoriatics (7 males and 4 females) in the age range 21 to 62 years, were studied. All had had psoriasis for several years with an unsatisfactory response to conventional therapeutic agents, including topical steroids, tar, ultraviolet light, and systemic methotrexate. Only chronic stable plaques were treated; other medications were discontinued at the start of this study.

Psoralen. 4,5′,8-trimethylpsoralen powder was dissolved in a 50 : 50 (v/v) mixture of absolute ethanol and propylene glycol to make 4 concentrations: 0.025%; 0.05%; 0.1%; and 0.25%. Solutions were stored in amber glass bottles which were wrapped in aluminum foil. New solutions were made at least monthly.

Black light. 4-General Electric F15T8-BLB black lights were mounted in two desk-top lamp-holders (luxolamp) with aluminum foil backing to increase reflectance. Spectral energy output of the black lights ranged predominantly between 330 and 390 nm with a peak near 360 nm (8). The lights, placed 15 cm from the skin during irradiation, gave an incident flux of approximately 8.2×10^3 ergs/cm²/sec as measured by a Yellow Springs Instrument radiometer.

Technique. Areas (20–80 cm² in diameter) within chronic plaque-type psoriatic lesions were selected on the trunk or extremities as test sites. Nearby areas, preferably in the same plaque, were used as controls and received either black light or psoralen alone. Prior to irradiation, patients used a calibrated syringe to apply a predetermined volume and concentration of psoralen solution to a measured area of a psoriatic plaque. The volume varied from 0.1 to 0.6 ml depending on the area treated, while the concentration used initially was usually 0.025% and then increased with further treatment. The dose of psoralen per skin area varied from a starting concentration of approximately 0.2 μg/cm² to a final concentration as high as 2.0 μg/cm². Absolute alcohol/propylene glycol base was applied to control areas which were to receive black light alone. Two hours later these sites were irradiated with black light under our supervision in an out-patient clinical setting starting with 5 minutes exposure and increasing to as long as 30 minutes on subsequent visits. In 6 of 11 patients, psoralen-treated sites were used as controls and covered with aluminum foil during irradiation.

Our initial studies showed that the psoralen + black light combination produced a maximum erythema in normal skin by 48 to 72 hours. We therefore decided to irradiate 3 times weekly. Total treatment time was a 3

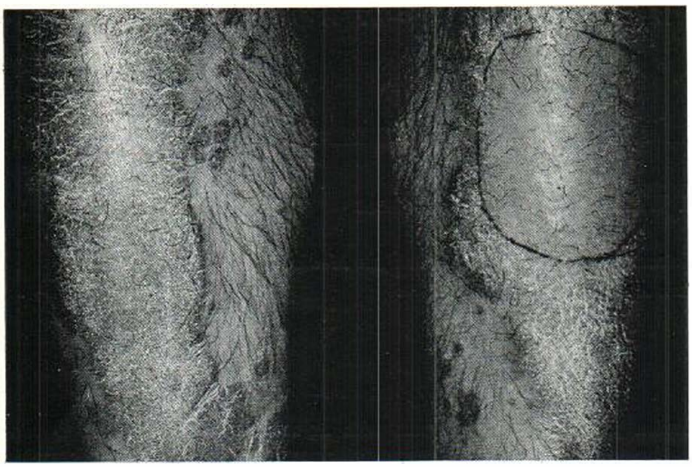

Fig. 1. Psoriatic plaque (on the front of the lower leg, an area frequently the last to clear on conventional therapy) 10 days after termination of treatment. Note flattened area with distinct border where psoralen plus black light has been used. This patient falls in the "much" category in Table I.

to 4 week period with follow-up 2 to 4 weeks after stopping treatment. Patients were told to avoid sun or artificial ultraviolet exposure to the areas between visits.

Responses in all patients were evaluated by us at the time of each black light treatment and photographs taken before, during and after completion of therapy. Biopsies of experimental and control sites were performed on 3 patients at the termination of their treatment period.

Design of study. The intention in this pilot study was to establish whether or not psoralen plus black light could improve a psoriatic lesion, rather than to arrive at a definitive treatment regimen. Therefore this preliminary effort was designed to run over a 3 to 4 week treatment period with a short-term follow-up. By using paired experimental and control sites on the same or nearby psoriatic plaques, we felt that improvement due to spontaneous resolution would be minimized.

RESULTS

As shown in Table I, 8 of 11 patients showed improvement in the psoralen plus black light treated lesions in comparison with black light or psoralen alone. This was apparent clinically by thinning of plaques, decreased scale (Fig. 1) and complete clearing in 2 of the 8 improved patients. Fig. 2 compares, in the same subject, the histological changes occurring in lesions treated with psoralen plus black light, black light alone, and psoralen alone. In general, plaques continued to improve 7 to 10 days after stopping treatment but then tended to recur 2 to 4 weeks later. All black-light-alone and psoralen-alone test sites remained unchanged as compared either with photographs taken of the lesion before therapy, or with surrounding untreated plaques.

Three of 11 psoralen plus black light treated patients did not improve but rather demonstrated a Koebner phenomenon. One became considerably worse from the start, with erythema, burning, and pustules at the site. The other 2 patients improved initially but then developed increased scale after 1 week of treatment. Other untoward effects observed in several patients included occasional bulla formation and pigmentation.

Table I. *Improvement of psoriatic plaques exposed to psoralen plus black light*

Areas treated	Response at each plaque[a]			Number of patients observed	% improvement
	Much	Some	None		
Psoralen plus black light	4	4	3	11	73
Black light	0	0	11	11	0
Psoralen	0	0	6[b]	6	0

[a] Response: Much: good to excellent improvement; Some: mild to moderate improvement; None: no improvement. This grading system is not meant to evaluate duration of remission but only the response of the plaque.
[b] 6 of 11 patients had a psoralen control.

DISCUSSION

Although a statistical analysis suited to this particular type of study cannot be done properly with a sample size of 11 patients, these data do strongly suggest that psoralen plus black light has the ability to improve psoriatic lesions. This finding agrees with work first described by L. Harber and presented by Allyn in 1962 (1) in which a phototoxic reaction to psoralen involuted psoriatic plaques. Presumably this favorable response occurs via inhibition of DNA synthesis in the lesion similar to that previously shown in

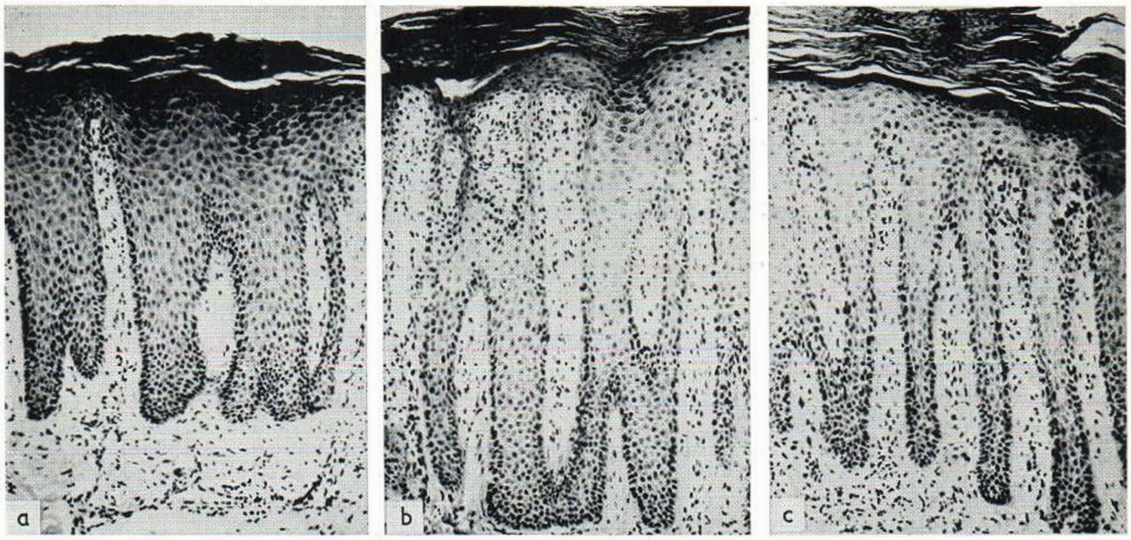

Fig. 2. Histological changes after 3 weeks' treatment in a psoralen plus black light treated area (*a*) as compared with black light (*b*) or psoralen (*c*) control areas. In the psoralen plus black light treated lesion (*a*) the epidermis shows decreased acanthosis, a loss of parakeratosis, and an increase in the number of cells containing keratohyalin (hematoxylin-eosin, original magnification × 80).

vitro (10). Since the sole purpose of this study was to determine whether psoralen plus black light could improve psoriatic lesions, the fact that the response was not complete in all patients, and was followed by a relapse, may or may not have some relevance to possible future therapeutic potential.

Because this report shows that psoralen plus black light can afford improvement, a definitive study designed to determine the optimum treatment regimen appears to be indicated. Such a study should evaluate various concentrations of psoralen and black light exposure times, larger treatment areas, intervals between treatment, total duration of therapy, and longer follow-up, to establish if a patient could obtain several months' remission after the most efficacious program possible. Because the pattern of epidermal differentiation after psoralen and black light was not yet completely normal in our patients (Fig. 2 is an example), it would be important to correlate any proposed treatment schedule with histology. Intuitively we suspect that a correlation might exist between the length of remission and the extent of residual histopathology at the termination of treatment. Also of interest would be a simultaneous comparison of effectiveness of psoralen plus black light with the currently popular (except with many patients) and effective Goeckerman regimen. Psoralens are not as messy as crude coal tar and would be more acceptable for office and outpatient treatment as well as in-patient therapy.

Cutaneous activation of psoralens with black light should avoid deleterious effects on other rapidly proliferating cells of the body and allow more precise control over the areas to be treated. Black lights by themselves do not produce a sunburn effect. Thus, a psoralen + black light combination with shielding of surrounding normal areas might be used in a fashion similar to the dermatologic office X-ray machine, but without the other potential problems of X-irradiation.

The major disadvantage of this form of therapy would be the possibility of producing a severe burn. The one patient who did considerably worse in our study had been started on the highest concentration of psoralen, e.g. 0.25%, with black light exposure as long as 30 minutes. Dilute solutions, e.g. 0.025%, applied over small areas without occlusion in conjunction with 5 minutes or less of black light exposure should be used initially to evaluate each patient's response. Pigmentation also occurred at treated sites but the patients have not been followed long enough to determine if prolonged hyperpigmentation would be a significant deterrent to this type of therapy for psoriasis. Bulla formation and pigmentation appeared to relate directly to the use of increased

concentrations of psoralens and prolonged black light exposure. Benzophenone sun screens applied over treated areas between visits may help avoid an added effect from the sun or other ultraviolet light sources while the patient is using psoralens (6).

In conclusion, this study supports the idea that topical psoralens plus black light may have therapeutic value in psoriasis. Since inhibition of DNA synthesis in uninvolved areas (an event which presumably takes place to some extent in patients on systemic methotrexate) does not seem to interfere significantly with epidermal integrity, it is conceivable that oral psoralen could be given intermittently in a dose sufficient, along with appropriate black light exposure (possibly including some shielding), to afford significant improvement of lesions and minimum phototoxicity in uninvolved areas. This pilot study, the preliminary report of Tronnier & Schüle (8), and the sound biochemical rationale on which our study was based (10) suggest that further critical evaluation of a topical or systemic psoralen + black light treatment combination for the intermittent mitigation of psoriasis would be appropriate.

ACKNOWLEDGEMENTS

This investigation was supported in part by general research support grant RR-05383-09, American Cancer Society institutional research grant IN-40J, the Irene Heinz and John LaPorte Given Foundation and NIH grant AM-15740-01.

M. Anthony Schork, Ph.D., Department of Biostatistics, University of Michigan, provided statistical assistance.

REFERENCES

1. Allyn, B.: Studies on phototoxicity in man and laboratory animals. Presented at the 21st annual meeting of the American Academy of Dermatology, December 1–6, 1962, Chicago, Illinois.
2. Baden, H. P., Parrington, J. M., Delhanty, J. D. A. & Pathak, M. A.: DNA synthesis in normal and xeroderma pigmentosum fibroblasts following treatment with 8-methoxypsoralen and long wave ultraviolet light. Biochim Biophys Acta *262:* 247, 1972.
3. Epstein, J. H. & Fukuyama, K.: A study of 8-methoxypsoralen (8-MOP) induced phototoxic effects on mammalian epidermal macromolecular synthesis in vivo. J Invest Derm *54:* 350, 1970.
4. Leavell, U. W., Jr & Yarbro, J. W.: Hydroxyurea. A new treatment for psoriasis. Arch Derm (Chicago) *102:* 144, 1970.
5. Mandy, S., Taylor, J. R. & Halprin, K.: Topically applied mechlorethamine in the treatment of psoriasis. Arch Derm (Chicago) *103:* 272, 1971.
6. Parrish, J. A., Pathak, M. A. & Fitzpatrick, T. B.: Prevention of unintentional overexposure in topical psoralen treatment of vitiligo. Arch Derm (Chicago) *104:* 281, 1971.
7. Rees, R. B., Bennett, J. H., Maibach, H. I. & Arnold, H. L.: Methotrexate for psoriasis. Arch Derm (Chicago) *95:* 2, 1967.
8. Tronnier, H. & Schüle, D.: First results of therapy with long wave UV after photosensitization of skin, in Schenck GO (ed): Book of abstracts, symposia, and contributed papers, Sixth International Congress of Photobiology. Bochum, August 21–25, 1972, p. 340.
9. Tsuji, T. & Sugai, T.: Topically administered fluorouracil in psoriasis. Arch Derm (Chicago) *105:* 208, 1972.
10. Walter, J. F., Voorhees, J. J., Kelsey, W. H. & Duell, E. A.: Psoralen plus black light inhibits epidermal DNA synthesis: Arch Derm (Chicago) *107:* 861, 1973.
11. Weinstein, G. D. & Frost, P.: Abnormal cell proliferation in psoriasis. J Invest Derm *50:* 254, 1968.

Received March 7, 1973

J. J. Voorhees, M.D.
Department of Dermatology
The University of Michigan Medical School
Ann Arbor, Michigan 48104
USA