PUVATHERAPY FOR PSORIASIS AND OTHER SKIN DISEASES
AN INITIAL REPORT

by

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SUMMARY

Fifty-two patients with severe and resistant psoriasis were treated with 8-methoxypsoralen followed by high intensity long wave ultraviolet light over a 12-month period at the Royal Victoria Hospital, Belfast. One hundred per cent clearing of the plaques of psoriasis was obtained with an average dose of energy of 53.5 joules in 43 (96 per cent) of 45 patients and the other two materially improved. Seven are still in the clearing phase. Early side effects were uncommon. There was no clinically significant change in laboratory or ophthalmological findings. Of the nine patients who complained of arthritis, four had radiological evidence and one showed radiological improvement after PUVA. In this study all seven patients who had been using large doses of topically applied steroid cream (up to 200 g Dermovate per week for two years) did not show adrenal suppression.

INTRODUCTION

Although the precise cause of psoriasis is unknown the characteristic lesions are associated with epidermal proliferation and increased enzymatic and metabolic activity. Attempts to control the rapid replication of cells by local application of cytotoxic agents such as 5-thiouracil and nitrogen mustard have been largely unsuccessful. Systemic cytotoxic agents, in particular methotrexate, have been more successful. They inhibited DNA synthesis and thus provided a stimulus in the search for other less toxic inhibiting agents. Psoralens in the presence of UVA (320-400) were seen to inhibit DNA synthesis (Walter et al, 1973) and this was extended when Parrish et al (1974) and later Wolff et al (1975) reported successful treatment of psoriasis using the technique of photochemotherapy. This involved the oral administration of 8-methoxypsoralen (8-mop) followed by exposure to high intensity long wave ultraviolet light. This was an excellent combination of two treatments, neither of which was effective on its own, producing synergistic results. The spectrum of psoralens and photosensitization lies within the UVA range, and as UVA requires 100 times more energy than UVB to produce erythema this enables a more prolonged therapy. The treatment was introduced in the Royal Victoria Hospital, Belfast, in September, 1977, and the following is a report of a trial over one year.
EXPERIMENTAL PROCEDURE

Selection of patients

Patients were selected for the trial under four groups:

Group A: patients unresponsive to conventional tar and dithranol therapy.
Group B: patients who had received large amounts of topically administered steroids in whom it was hoped to prevent a flare-up when treatment was abruptly discontinued.
Group C: patients receiving methotrexate with anticipation of withdrawal of the drug.
Group D: patients with psoriasis confirmed to palms of the hands and soles of the feet.

In addition, only those over the age of 18 were included in the trial.

Dosage of 8-methoxypsoralen

The drug was given to each patient on a weight related basis as shown in the following schedule (Table 1).

| Weight of patient (kg) | Dose of 8-MOP (mg) |
|------------------------|--------------------|
| <30                    | 10                 |
| 30—50                  | 20                 |
| 51—65                  | 30                 |
| 66—80                  | 40                 |
| 81—90                  | 50                 |
| 90+                    | 60                 |

Equipment for UVA radiation

The system chosen was a Waldeman PUVA, 6,000 for a whole body radiation with the Waldeman 200 for hands and feet.

Measuring the sensitivity of individual patients

This was done subjectively by skin typing and objectively by phototesting. Skin typing was determined as shown in Table II.

| Skin type | History                           | No. of patients |
|-----------|-----------------------------------|-----------------|
| 1         | Always burn, never tan            | 13              |
| 2         | Always burn, sometimes tan        | 17              |
| 3         | Sometimes burn, always tan        | 19              |
| 4         | Never burn, always tan            | 3               |
Phototesting was performed on each patient. The minimal phototoxicity dose (MPD) is the dose which produces barely perceptible but well defined erythema. However, this does not forecast the patient's capacity to tan. Therefore a patient with a high MPD and at a low sensitivity may tan very slowly and so produce erythema to even small increases in UVA. As adjustments are necessary because of increased tolerance to initial UVA dosage it is helpful to know the patient's ability to develop pigmentation with respect to erythema. This is calculated as a photosensitivity pigmentation index (PPI) as in Table III. As PPI

\[
\text{PPI} = \frac{\varepsilon \text{E}72 + \varepsilon \text{P}120}{\varepsilon \text{E}72 + \varepsilon \text{P}120}
\]

Where
- \(\varepsilon \text{E}72\) is the sum of all erythema readings at 72 hours.
- \(\varepsilon \text{E}120\) is the sum of all erythema readings at 120 hours.
- \(\varepsilon \text{P}72\) is the sum of all readings for pigmentation at 72 hours.
- \(\varepsilon \text{P}120\) is the sum of all readings for pigmentation at 120 hours.

increases above 1 the greater the possibility of burning and consequently as it decreases below 1 the greater the possibility of developing tolerance.

*Treatment schedule*

Each patient received treatment three times per week. There were three variables, psoralen ingested, the UVA radiation and the patient's sensitivity to PUVA. In the trial psoralen was kept constant on a weight related basis and the other two factors were adjusted according to the individual response. The initial dose of UVA was the minimal phototoxicity dose and those increments were calculated from the PPI. When clearing was complete the patient was placed on maintenance therapy, initially twice per week, reducing in some cases to one treatment every two months. This interval was not exceeded as at this stage the lesions developed accounting for not more than 5 per cent of the body surface. The patient accepted these but it was felt that further reduction would result in more widespread lesions. If the patient on maintenance PUVA developed psoriasis on 5 per cent or more of the skin surface, he was restored to thrice weekly treatment with a dose of UVA as for last maintenance exposure. This was increased as required.

*Laboratory tests*

Each patient had the following tests performed prior to commencing PUVA therapy:— full blood picture, differential white cell count, erythrocyte sedimentation rate, block analysis – this included serum sodium, potassium, chloride, carbon dioxide, urea, calcium, cholesterol, glucose, bilirubin, alkaline phosphatase, AST, ALT, total protein, albumin, uric acid, creatinine, creatine phosphokinase, lactate dehydrogenase, iron and triglycerides. All these tests were repeated after
six PUVA treatments, then after 12 and thereafter monthly or more frequently depending on the uniformity of the results. The patient had a complete ophthalmological examination initially, after six months and subsequently at six-monthly intervals or earlier if requested by the ophthalmologist.

RESULTS

Table IV showss that satisfactory clearing of the lesions was obtained in patients in Groups A, B, and D, and indicates the frequency and dose required to produce this outcome. It compares the results as regards number of exposures and dosage with those in the literature. Satisfactory results have been obtained here with a lower level of radiation.

Some more resistant cases are in the five in Group C who had been treated with methotrexate. Three with psoriasis of 4 months, 21 and 22 years and treated for 4 weeks, 2 years and 1½ years with 7.5, 10.0 and 2.5 mg weekly, responded to treatment comparable to those in Groups A, B and C. One affected for 30 years and treated with 7.5 mg methotrexate weekly for 1½ years, although he has now responded, required PUVA therapy for one year. The other patient with psoriasis for 23 years had been treated with 15 mg weekly for two years and failed objectively to respond to PUVA.

TABLE IV

Results of PUVA therapy in groups A, B, D, and results recorded by Melski et al and Wolff et al

| Group   | No. of patients | Average No. of exposures | Joules/cm² at last clearing | Average No. of joules/cm² to produce clearing |
|---------|-----------------|--------------------------|-----------------------------|-----------------------------------------------|
| A       | 20              | 23.52                    | 55.35                       | 4.15                                          |
| Melski et al | 23.6          | 251.0                    | 11.8                        |                                               |
| Wolff et al  | 13.39 ± 7.08  | 66.1 ± 56.7              | —                           |                                               |
| B       | 11              | 21.75                    | 68.7                        | 3.8                                          |
| D       | 9               | Hands 19.00              | 47.0                        | 3.6                                          |
|         |                 | Feet 32.0                | 117.7                       | 4.7                                          |

DISCUSSION

The dermatologists decided that the day-to-day management of the machine would be best carried out by physiotherapists in their department and this has worked well. The patients are routinely reviewed and their therapy regulated by a dermatologist. The number of joules required to produce clearing in association with the mean joules per cm squared at the last treatment compared to the results obtained by Melski et al (1971) and Wolff (1978) is shown in Table IV.

The complications as a result of therapy may be short-term or long-term. Short-term side effects which had been expected and those found in our series are shown in Table V. The most troublesome side effect in the short-term was
pruritus. This, however, was easily controlled by an antihistamine. Nausea was also a prominent symptom but again disappeared when PUVA was continued. Long-term side effects must include eye complications such as cataracts and skin cancer. No opinion about either may of course be given after one year's therapy. There is still no evidence of skin neoplasm in any patient after treatment for two years with PUVA.

All laboratory results showed no variation after PUVA therapy and it can be concluded that PUVA in the short-term does not materially alter renal or hepatic function. Of interest is the subjective improvement in arthritis noted in five patients and in one of these there was radiological evidence of improvement. It is also of note that three patients, all of whom were male, noted excessive hair growth (anterior chest, beard area). The nail growth was measured for each of these three men and was found to be within normal limits. The plasma testosterone was also within normal limits for all patients. Of note, none of the patients in this series showed the expected exacerbation when the topical corticosteroids were abruptly discontinued and none showed evidence of adrenal suppression even when applying Dermovate 200 g per week for two years.

CONCLUSION

PUVA is obviously a beneficial and effective therapy but what is worrying and unpredictable in a long-term skin carcinogenic effect in view of its action on DNA (Stern et al 1979). In this series 100 per cent clearing was obtained with an average dose of energy of only 53.5 joules as compared to 251 joules (Melski et al 1977) (see Table IV). None of the patients developed skin cancer and this may be related to the lower dosage, but in addition no patient had a history of previous skin neoplasm or radiation therapy. There is also the possibility of an effect on elastic tissue, producing premature ageing. While these complications remain uncertain the treatment must be kept under careful medical control, and obviously as a low dose of energy can produce 100 per cent clearing it is prudent to treat the patients with this lower dose regime. At the moment there is no place for it as a home therapy.
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