Topical psoralen photochemotherapy (PUVA) and superficial radiotherapy in the treatment of chronic hand eczema

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SUMMARY

The therapeutic efficacy of conventional superficial radiotherapy and topical psoralen photochemotherapy (topical PUVA) administered over a 6 week period was compared in a double-blind study of 21 patients with chronic bilateral constitutional hand eczema. One hand was treated with conventional superficial radiotherapy and the other with topical 8-methoxypsoralen and long-wave ultraviolet light (topical PUVA). Significantly better clinical improvement was seen in superficial radiotherapy treated hands over topical PUVA treated hands after 6 weeks of treatment, but this difference was not maintained at 9 or 18 weeks. There was no significant difference in symptom severity between the two treatments after 6 weeks, but superficial radiotherapy produced significantly more symptomatic improvement at 9 and 18 weeks. Superficial radiotherapy is a less time consuming procedure than topical PUVA and leads to more rapid improvement.

Chronic constitutional hand eczema is a debilitating disorder which is often resistant to topical medication. Superficial radiotherapy is established as an effective treatment for chronic hand eczema resistant to conventional topical measures.1,2

Recent studies have suggested that oral psoralen photochemotherapy (PUVA) may be useful in the treatment of chronic dermatitis of the hands.3-7 Topical PUVA avoids the potential problems of systemic administration of psoralen and has been used successfully to treat a number of conditions confined to the palms and soles, in particular psoriasis.8 Topical PUVA has not been evaluated in the management of chronic hand eczema.

We therefore undertook to evaluate the role of topical PUVA in the treatment of chronic constitutional hand eczema. In this study we chose to compare topical PUVA with superficial radiotherapy rather than placebo because superficial radiotherapy is already established as an effective treatment.1,2

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METHODS

Patients
Twenty-five patients with bilateral and symmetrical chronic constitutional palmar eczema were entered into the study. All patients had chronic eczematous changes on the palms for at least 6 months with either continuous or episodic vesiculation. Twenty-one patients completed treatment. Fourteen were female and seven were male and their mean age was 52.3 years (range 19–79 years). All patients were resistant to conventional therapy with topical emollients, steroid and tar preparations. Patients with irritant and contact allergic dermatitis were excluded by a detailed history and by patch testing with the European standard battery plus additional materials where indicated.

Treatments
Patients were randomly allocated topical PUVA to one hand and superficial radiotherapy to the other using a pre-determined code. Treatment with emollients and either topical steroid or tar preparations was continued unchanged to both hands throughout the study.

The superficial radiotherapy was administered by a Dermopan II X-ray machine using a 1 mm aluminium filter and a lead applicator to maintain a focal distance of 30 cm. One hand was irradiated with 0.9 Gy at 50 KV administered on three occasions at 21 day intervals. The topical PUVA treated hand received sham radiotherapy during which the X-ray machine appeared to function normally but the power supply to the tube was interrupted such that no X-rays were received by the patient. During treatments the patient wore a protective lead apron from the neck to the knees.

Topical PUVA was administered by application of 1%, 8-methoxypsoralen in an organic solvent base (Deltasoralen, Delta Laboratories Ltd, Dublin, Eire) to affected areas on the non-radiotherapy treated hand. The psoralen was applied 5 min prior to long-wave ultraviolet (UVA) exposure. A short interval between application of psoralen and UVA exposure was chosen because this was more convenient for patients and allowed more accurate application by trained nursing staff. The epidermal penetration of 8-methoxypsoralen is rapid and previous studies in patients with psoriasis have shown that a short interval of 5–10 min between application of topical psoralen and exposure to UVA is as effective as longer intervals of up to 2 h. The UVA was administered using a Blacklight HF1 unit as a light source. Exposure was started at 2 J cm⁻² and increased gradually to a maximum of 15 J cm⁻². The hands were washed thoroughly with emulsifying ointment immediately after UVA exposure. Treatments were given three times a week for 6 weeks.

The superficial radiotherapy treated hand was treated with a sham PUVA procedure. This consisted of an application of the organic solvent base without psoralen 5 min prior to exposure to the light source. In addition, a 6 mm perspex filter was inserted between the hand and the light source which effectively reduced UVA transmission by more than 90%. The procedure was carried out in such a way that patients were unable to tell which hand had received active treatment.

Assessments
Patients were assessed by two observers (R.S-D and M.G) who were unaware of the treatment status of each hand until the codes were broken at the end of the study. Assessments were made prior to treatment and at 6, 9, and 18 weeks after starting treatment. A severity grade was assigned for each hand: Grade 0, normal skin; Grade 1, mild scaling and erythema; Grade 2,
moderate scaling, erythema and shallow fissures; Grade 3, severe scaling, erythema and deep bleeding fissures; Grade 4, active pomphlyx. In addition the patients were asked to indicate the severity of symptoms on a 10 cm linear analogue scale.

Statistical analysis was by Wilcoxon ranked pairs tests.

RESULTS

Of the patients entered into the study, four patients failed to complete the treatments and to attend for subsequent follow up. Of the patients who completed treatment, assessments were obtained for all 21 patients at 6 and 9 weeks and for 20 patients at 18 weeks. One patient failed to attend for the 18 week follow up assessment.

The mean clinical severity scores for superficial radiotherapy and topical PUVA treated hands are shown in Figure 1. There were significant improvements from pre-treatment scores for both treatment modalities at the 6, 9 and 18 week assessments. Superficial radiotherapy was significantly better than topical PUVA at 6 weeks ($P = 0.014$) but this difference was not maintained at the 9 and 18 week assessments.

The mean symptom severity scores for superficial radiotherapy and topical PUVA are shown in Figure 2. Again there were significant improvements for both treatments at the 6, 9 and 18 week assessments. Symptom severity scores were lower for superficial X-ray treated hands than topical PUVA treated hands at 6, 9 and 18 weeks. The difference was statistically significant at 9 weeks ($P = 0.046$) and 18 weeks ($P = 0.013$), but not at the 6 week assessment.

![Figure 1](image1.png)

**Figure 1.** Mean clinical severity scores for superficial radiotherapy and topical PUVA treated hands.

△——△, superficial radiotherapy; ■——■, Topical PUVA.
FIGURE 2. Mean symptom severity scores for superficial radiotherapy and topical PUVA treated hands.

- ▲, superficial radiotherapy; ■, Topical PUVA.

DISCUSSION

Superficial radiotherapy has been shown to be of benefit in the treatment of chronic hand eczema in two placebo controlled studies. Fairris et al.\(^1\) demonstrated that superficial radiotherapy gave significantly better results than placebo. The effect was maximal 6–9 weeks after initiation of treatment but persisted at 18 weeks. King and Chalmers\(^2\) found that superficial radiotherapy gave significantly better results than placebo 7 weeks after initiation of treatment; results were better at 3 and 6 months but the differences did not reach statistical significance.

PUVA with oral psoralen has been successfully used to treat generalized constitutional eczema.\(^12\) Uncontrolled studies have reported benefit from oral PUVA in chronic dyshidrotic hand eczema,\(^3\) chronic hyperkeratotic dermatitis of the palms,\(^4\) chronic contact allergic\(^3\) and irritant dermatitis.\(^4\) One open controlled study has shown benefit from oral PUVA in patients with chronic dyshidrotic eczema of the palms.\(^7\) Topical psoralen in PUVA treatment has been found to be effective for conditions affecting the palms and soles, such as psoriasis,\(^8\) and avoids many of the potential problems produced by oral administration of the drug. The use of topical PUVA therapy in the treatment of chronic hand eczema has not previously been evaluated.

We have shown that topical PUVA and superficial radiotherapy are both effective over a period of 2 months in the treatment of chronic constitutional hand eczema. Improvement was more rapid with superficial radiotherapy. Superficial radiotherapy produced a more significant improvement in symptom severity than topical PUVA at 9 and 18 weeks after the start of treatment. Safe guidelines have been established for the use of superficial radiotherapy in benign dermatoses.\(^13\) It is recommended that the total lifetime dose of conventional superficial
radiotherapy should not exceed nine Gy (approximately three courses of the regime used in this study). This provides a substantial margin of safety particularly for relatively radio-insensitive sites such as the palms and soles.

The frequent attendance required for topical PUVA therapy caused some difficulty for several of our patients and this could lead to poor compliance with treatment. The application of the psoralens in an organic solvent base was painful in some patients with fissures of the skin though only transiently, but this discomfort could reduce compliance and the solvent base may have a deleterious effect on dry eczema. This might be avoided by use of an alternative vehicle for administering the psoralen.

The advantages of superficial radiotherapy over topical PUVA make superficial radiotherapy a better choice for treating chronic hand eczema. However, topical PUVA is a useful alternative treatment and should be considered where superficial radiotherapy is not available or where the maximum lifetime dose of superficial X-rays have been given.

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REFERENCES