

## CONTROLLED DOUBLE BLIND TRIAL WITH SUPRACORTIN CREAM

By V.S. Rajan

Atopic dermatitis and lichen simplex chronicus are endogenous eczemas which present therapeutic problems due to their chronicity.

Topical corticosteroids have been successfully used in the treatment of these dermatoses for many years. The development of new steroids and improved vehicles have considerably extended possibilities in improvement of topical therapy. Years of experience have shown that long-term therapy can lead to local and/or systemic side effects. This problem appears particularly in children and patients with widespread disease. In order to achieve a balance between effectiveness and untoward side effects steroid therapy should be used only in absolutely necessary doses. Preparations which ensure a prolonged anti-inflammatory effect due to the accumulation of the steroid in the skin will reduce the number of applications and the total amount of steroids applied.

By means of experimental and clinical investigations a depot effect of this kind was proved for fluprednylidene-21-acetate in cream base (Hopsu-Havu and Tuohima, 1970; and Luecker *et al*, 1968). Moreover, the cream base was shown in controlled investigations to promote healing of the skin damaged by inflammation (Borelli *et al*, 1975; Schneider and Koch, 1974; and Tronnier *et al*, 1975). Alternating use of fluprednylidene-21-acetate and the steroid-free cream base (Freshwater, 1974; Garrets, 1975; and Milbradt, 1971), was shown to enhance its therapeutic effect.

This trial, on patients with atopic eczema and lichen simplex chronicus was conducted to demonstrate whether once daily application of fluprednylidene-21-acetate in cream base was equally efficacious as thrice daily application of the well-proven topical corticosteroid, betamethasone-17-valerate. In order to maintain conditions of a double blind trial, and to guarantee in every case, the application of the cream three times daily, treatment with fluprednylidene-21-acetate once daily was supplemented with two daily applications of the steroid-free cream base.

### PATIENTS AND METHODS

For the trial all preparations were filled into identical tubes. Each patient was given two coded tubes, with instructions to apply once daily and twice daily.

The tubes to be used once daily contained either fluprednylidene-21-acetate or betamethasone-17-valerate cream and the tubes to be used twice daily contained either the steroid-free cream base or betamethasone cream.

58 patients (17 males, 41 females) from Middle Road Hospital with a diagnosis of atopic dermatitis (N=18) or lichen simplex chronicus (N=40) were treated thrice daily according to instructions. The average age of the patients was 30 years. Neither the attending physician nor the patients knew the composition of the individual tubes dispensed. The code and patient's registration number were recorded on the trial sheet. Decoding took place after the trial was over.

Decoding showed that 30 patients were treated once daily with fluprednylidene-21-acetate cream and twice daily with the steroid-free cream base and 28 patients thrice daily with betamethasone-17-valerate cream.

The average duration of the trial was 15 days for all patients. On admission to the trial, the patients' age, sex, diagnosis and distribution of the dermatosis was recorded on the trial sheet. Also pruritus, erythema, lichenification, nodules, scaling, crust formation and other signs were recorded and their intensity graded as follows:

- 0 = Absent
- 1 = Mild
- 2 = Moderate
- 3 = Severe

Patients were seen at the end of one and two weeks and reassessed. At the end of the trial, all the data registered were transferred to punch cards and statistically evaluated.

### EVALUATION AND RESULTS

Since the trial was mainly intended to compare two therapy patterns, regression of the signs and symptoms within the trial period was the only parameter used for comparison.

For evaluation, the symptomatology score for each patient calculated prior to and after treatment was completed by adding the scores recorded. Mean

---

Middle Road Hospital.

DR. V.S. RAJAN, A.M., M.B., B.S., M.R.C.P. (Edin.), M.R.C.P. (Glas.), Dip. Derm. (Lond.), Senior Physician.

---

TABLE I  
COMPARATIVE STATISTICAL EVALUATION OF THE DOUBLE BLIND TRIAL

		Fluprednylidene-21-acetate cream once daily and cream base twice daily	Betamethasone-17- valerate cream thrice daily
Number of Cases		30	28
Symptomatology score * prior to start of the trial	Mean value	12.7	12.3
	Standard deviation	4.2	3.7
Symptomatology score after 14 days of treatment	Mean value	7.4	8.5
	Standard deviation	3.8	3.7
Change in score	Mean value	-5.3	-3.8
	Standard deviation	3.6	4.6
	t	-8.06	-4.3
	p<	0.01	0.01
Adjusted final values		7.3	8.6

\* Symptomatology score = sum total of the intensity of signs and symptoms recorded.  
Result from the covariance analysis:  $F = 1.94$  ( $df_1 = 1$ ;  $df_2 = 55$ )  
 $p = 0.17$

values and standard deviations were determined for both groups.

A change in the score after treatment was used to statistically evaluate the therapeutic effectiveness of the chosen treatment schedule (Table I).

Statistical evaluations showed that the initial values for both groups were approximately the same and comparison between the two groups possible.

The reduction in the symptomatology score is statistically significant (t test for independent groups) for both therapy schedules.

Evaluation of the two modalities of treatment showed no statistically significant superiority of either modality.

#### DISCUSSION

To minimise defaulters amongst those admitted the trial had to be limited to a two-week period. Though short the period was adequate to show statistically significant regression in signs and symptoms. It is possible better results would have been obtained if the length of the trial period was extended.

As shown in other trials (Garrets, 1975), this study has again shown that therapeutically, fluprednylidene-21-acetate in a special cream base (Supracortin) applied once daily and supplemented twice with only the cream base was as effective as applying betamethasone-17-acetate thrice daily.

The advantages therapeutically are:

1. Smaller quantities of a potent steroid preparation are applied with fewer possible side effects.
2. Conservation of time for the patient with no loss of therapeutic efficiency.

The favourable therapeutic response obtained with fluprednylidene-21-acetate in a special cream base is to a large extent attributable to its cream base. It not only permits the steroid to form a depot in the skin but promotes active healing of the diseased epithelium. Thus in more acute states, the once daily application of the steroid, supplemented with the twice daily application of the cream base enhances recovery.

#### SUMMARY

In a controlled double blind trial in patients with atopic dermatitis and lichen simplex chronicus two modalities of topical therapy were compared.

One group of patients ( $N = 30$ ) was treated once daily with fluprednylidene-21-acetate and twice daily with the corticoid-free cream base.

A second comparable group ( $N = 28$ ) was treated with thrice daily applications of betamethasone-17-valerate cream.

Statistical evaluation of the regression of signs and symptoms recorded after 14 days of treatment showed statistically no significant differences for both groups ( $p < 0.01$ ).

## ACKNOWLEDGEMENTS

Our sincere thanks to E. Merck, Darmstadt, Germany, for supplying the fluprednylidene-21-acetate in special cream base (Supracortin) for the trial.

## REFERENCES

1. Borelli S., Gehrken H. and Koch E.: "Double-blind comparative investigation of two topical skin care preparations in chronic recidivating dermatoses." *Der Informierte Arzt*, 1, 12-18, 1975.
  2. Freshwater D.G.: "Comparative investigations with fluprednylidene acetate." *Medikon*, 5, 16-18, 1974.
  3. Garrets M.: "Controlled double-blind comparative trial with fluprednylidene acetate cream and its base." *Arch. Derm. Forsch.*, 251, 165-168, 1975.
  4. Hopsu-Havu V.K. and Tuohimä P.: "Quantitative and radioautographic studies on the penetration kinetics of 9 $\alpha$ -fluoro-16-methylene-prednisolone-21-acetate-7-T in human skin." *Arch. Klin. Exp. Derm.*, 239, 252-265, 1970.
  5. Luecker P., Nowak H., Stuetgen G. and Werner G.: "Penetration kinetics of a tritium-labelled 9 $\alpha$ -fluoro-16-methylene-prednisolone ester after epicutaneous application to humans." *Arzneim.-Forsch. (Drug Research)* 18, 27-29, 1968.
  6. Milbradt R.: "A double-blind semilateral trial to determine a therapeutically effective and safe dosage of fluprednylidene acetate cream." *Der Landarzt*, 47, 246-248, 1971.
  7. Schneider C. and Koch E.: "The effect of cream base IXa (Supracortin cream base) on toxic degenerative skin damage." *Berufs-Dermatosen*, 22, 225-264, 1974.
  8. Tronnier H., Weise K. and Koch E.: "Clinico-experimental investigations on the anti-inflammatory effectiveness of corticosteroids applied locally to human skin." *Der Hautarzt*, 26, 370, 1975.
- 
-