Diprosone Ointment in Psoriasis

A DOUBLE-BLIND TRIAL

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SUMMARY

A double-blind trial which compared the effects of two topical steroids on 58 successive cases of psoriasis is reported. The investigations compared the efficacy and cosmetic acceptability of betamethasone dipropionate ointment (Diprosone) with that of fluclorolone acetonide ointment (Topilar).

Under the conditions of the trial, the betamethasone dipropionate ointment in a concentration of 0,05% was significantly superior to 0,025% fluclorolone acetonide ointment in both the patient's over-all evaluation ($P<0,024$) and in the investigator's over-all evaluation ($P<0,008$); in the relief of pruritus noted by the patient ($P<0,063$) and in the degree of improvement in scaling observed by the investigator ($P<0,080$).

The phenomenon of sweating in patches of psoriasis is discussed.

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Topical corticosteroids are firmly established as the first line of treatment for inflammatory dermatoses. Nevertheless, no preparation yet available is completely effective and the search for better agents continues. This is particularly true of psoriasis. It can well be said that the discovery of any local application that would regularly relieve or even consistently improve that recalcitrant disorder would constitute a major therapeutic advance. The preparation reported on in this trial (Diprosone) is still not the long sought-after panacea. The findings, however, show that it is highly active and cosmetically acceptable, and that a high percentage of patients treated do show improvement while it is in use. Diprosone is therefore worth prescribing for any patient with psoriasis responding poorly to other forms of treatment, a situation only too frequently encountered.

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Betamethasone dipropionate has the chemical formula 9-fluoro-16- β-methylprednisolone-17, 21-dipropionate. As shown by the Stoughton-McKenzie vasoconstrictor response test,[1] it is effective at a concentration of 0,000016%, which is lower than that of any other steroid so tested.[2] The Stoughton-McKenzie test is used as a measure of the activity of locally applied steroid preparations, and the figure obtained indicates that Diprosone is an extremely active preparation.

PATIENTS AND METHODS

Patient Selection

Fifty-eight successive patients with psoriasis were studied; 30 were treated with Diprosone and 28 with Topilar. The majority of the patients (33) had had psoriasis for over 5 years and the condition was either static or exacerbating slowly. Of these patients, 50 had received prior therapy either with Synalar or with Betnovate ointment, with no more than temporary benefit.

No pregnant or lactating females and no patients with viral or tuberculous skin infections were included in the trial. No other local applications, no oral steroids and no oral antihistaminics were permitted during the trial, and none of the patients had been on them for at least a week before the trial.

Study Design

The patients were assigned at random in double-blind fashion to product A (Diprosone) or to product B (Topilar). Both preparations were supplied in 40-g tubes of identical appearance. The patients were instructed to apply the ointments twice daily, once in the morning

and once in the evening, and to massage them in lightly. Plastic occlusion was not used.

The patients were kept under observation for three successive weeks, and were re-examined by the same observer at weekly intervals during the trial. Their response was evaluated in respect of the relief of pruritus and in the disappearance of induration, inflammation (shown by redness), crusting and scaling.

Pruritus is a subjective symptom. The assessment of its severity and any degree of improvement is dependent on the patient's comments, although the presence or absence of scratch marks and bleeding points may guide the observer. It is sometimes thought that pruritus is not a prominent feature of psoriasis. This is by no means so. Lesions in many situations, in particular on the scalp, in the flexures and on the lower legs, may itch intolerably. A preparation's ability to relieve this symptom is consequently of value in assessing its usefulness.

Scaling is the end result of abnormal keratinisation. Its diminution, or in greater degree its control, is a visible indication that the preparation in use is modifying the excessive cell turnover and disordered granular layer formation characteristic of the disease.

At the final visit, the findings of the investigator and the comments of the patients in respect of all the parameters were taken into account, and an over-all assessment was made. The results were classified as much better, slightly better, no change, slightly worse or much worse, and were evaluated statistically by the technique of non-parametric statistical inference.[3]

Analysis of the data was carried out via the non-parametric Wilcoxon two-sample test.

RESULTS

Table I summarises the over-all findings of the trial.

TABLE I. OVER-ALL EVALUATION

	Diprosone		Topilar	
	Patient's evaluation	Doctor's evaluation	Patient's evaluation	Doctor's evaluation
Worse	**0**	**0**	**0**	**0**
No change ...	**1**	**2**	**0**	**1**
Slightly better ...	**5**	**5**	**14**	**17**
Much better ...	**24**	**23**	**14**	**10**

The significant contrasts are given in Table II.

TABLE II. SIGNIFICANT CONTRASTS ($P<0,10$)

Parameter	Visit	*P* value	In favour of Diprosone	In favour of Topilar
Patients' over-all evaluation	**Final**	**0,024**	**X**	
Investigator's over-all evaluation	**Final**	**0,008**	**X**	
Scaling	**Final**	**0,080**	**X**	
Pruritus	**Final**	**0,063**	**X**	

No other significant differences could be shown to exist ($P<0,10$).

Statistical analysis shows that under the conditions pertaining to this trial, Diprosone was significantly superior to Topilar in both the patient's evaluation ($P<0,024$) and the investigator's evaluation ($P<0,008$), and in the degree of improvement in scaling ($P<0,080$) and pruritus ($P<0,063$).

Side-Effects

There were 3 patients with side-effects from each drug. Two patients treated with Topilar complained of burning and 1 developed a boil on the right knee. One patient on Diprosone developed pustules in the scalp, 1 developed boils on the right leg and 1 developed transient, clear, superficial bullae on a sun-exposed area.

DISCUSSION

The nature of the bullae seen in the patient treated with Diprosone remains uncertain, but for the reasons given later, the fact that bullae appeared was taken to indicate that the preparation was therapeutically active. It was not looked upon as an undesirable side-effect.

The absence of sweating in patches of psoriasis which are not responding to treatment or which have not been treated; and the resumption of sweating in areas which have been cleared, are well-recognised phenomena. Shuster and Johnson[4] and Johnson and Shuster[5] have shown that there are two abnormalities of sweat gland function in the plaques of psoriasis: (*i*) superficial obstruction of the ducts leading to hypohydrosis; and (*ii*) an abnormality of absorption by the duct leading to inappropriately low sweat electrolyte concentration.

They were able to remove the duct blockage by complete cellophane stripping, and thereafter the sweat rate in the plaques of psoriasis was significantly greater than the rate in stripped clinically normal skin between the plaques. They concluded that this indicated a second defect in sweat gland function in the plaques; either an increased rate of secretion by the coil or a decreased rate of absorption by the duct. They proposed that miliaria occurred when the capacity of the coil to secrete was greater than the ability of the duct to absorb, and they noticed with surprise their inability to produce miliaria in stripped psoriasiform plaques after stimulation with pilocarpine in cases in which their findings showed impaired ductal absorption of water in relationship to $Na+$, $K+$, urea and possibly lactate. They concluded that this indicated that the capacity for ductal absorption, though impaired, still exceeded the rate of coil secretion.

If miliaria occur after the removal of psoriasiform scales by Diprosone, this may indicate one of three possibilities. Firstly, the clearing of the duct blockage may be more complete than that produced by stripping. Secondly, in addition to removal of the blockage, the Diprosone may stimulate secretion by the coil, and thirdly, the Diprosone may interfere with and thus reduce ductal absorption. A circumstance or set of cirumstances could therefore have resulted in which secretion was greater than absorption, and which led, in consequence, to the formation of miliaria.

It is thought on morphological grounds that the bullae were lesions of miliaria crystallina. Unfortunately, the patient refused biopsy and it is therefore possible to argue that they were sunburn blisters arising on pale areas with diminished melanin pigmentation. However, the absence of any marked tanning of, or desquamation from, the surrounding skin, which would presumably have followed a sunburn of a degree sufficient to produce blistering, is against such a diagnosis.

Subsequent experiments have been carried out in which attempts have been made to induce sweating in patches of untreated psoriasis and in patches treated with Diprosone. This was done by the subcutaneous injection of a dilute solution of mecholyl chloride (0,1 ml of a 1% solution) below the patches. Where the amount of sweating was estimated by the starch iodine test[6] a much greater degree of sweating was seen in patches which were treated by the application of Diprosone ointment before the injection of mecholyl chloride, than in patches which were not so treated.

The chemical composition of the increased sweat was not determined and it is not known if it was altered in any way. Changes in the electrolyte concentration might have indicated that the abnormality was in the absorptive function of the duct, but until further investigations have been carried out, it remains to be shown whether the action of Diprosone is principally one of clearing duct blockage, or whether it also influences coil secretion or duct absorption.

Both Diprosone and Topilar were criticised by the patients as being too greasy for routine use on their scalps, but the same property made them particularly effective and acceptable for use on dry scaly plaques on the trunk.

The absence of staining of skin and clothes made both products cosmetically acceptable to all the participants in the trial.

CONCLUSIONS

In this double-blind trial, 0,05% betamethasone dipropionate ointment (Diprosone ; Scherag) was found to be superior to 0,025% fluclorolone acetonide ointment (Topilar ; Syntex Rio) in the relief of pruritus, in the diminution of scaling, and, as judged by the over-all evaluation of the investigator and the patients, of its ability to control their disease. The findings were confirmed statistically.

REFERENCES

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