

From the Clinic for Allergic Diseases, Amsterdam, Netherland.

A POLICLINICAL STUDY OF
A NEW EXTERNAL CORTICOSTEROID
PREPARATION LOCACORTEN

By

W. J. F. VAN DER BIJL

It is now twelve years since corticosteroids were first introduced into dermatological practice and in the intervening period they have gained universal acceptance as most valuable agents, given both orally and topically, in the treatment of a wide variety of skin disorders. As a natural result of this wide interest in their use there has been an intensive programme of research, largely conducted by the pharmaceutical industry, to develop synthetic compounds which are ever more potent as anti-inflammatory agents whilst at the same time showing to the least possible extent those side effects which are inherently related to their basic structural activity.

A recent addition to this field is flumethasone pivalate (Locacorten). This synthetic corticosteroid is interesting in that it is the first doubly fluorinated prednisolone derivative which shows optimal activity in a lower concentration than other comparable preparations and which, furthermore, is cheaper. Optimal activity is obtained at a concentration of 0.02 per cent. A further point of interest is that the steroid is esterified with a pivalyl radicle to form the pivalate (trimethylacetate). This confers the property of rendering the molecule water insoluble and results in prolongation of local action when topically applied. Also, because of insolubility there is negligible systemic absorption, thus minimising the possibility of adreno-cortical suppression even when applied to large areas of skin.

So far, in the hands of the author, there has in no case been alteration of blood pressure, of the blood picture or of blood-sugar levels, nor has glycosuria been observed, in patients treated with Locacorten. There are, however, certain contraindications to its use, such as tuberculosis of the skin, syphilitic skin lesions and varicella, which apply to all corticosteroids. Locacorten formulations are not suitable for topical application to the eye.

Assessment: Assessment of the value of preparations for topical use can be very difficult and involves many pitfalls for the unwary physician.

First, there may be recurrences of the condition under study which are due not only to variations implicit in its natural history but also to such factors as the failure of the patient to follow accurately the doctor's instructions. Patients may also be continuing their own particular home remedies, unknown to the doctor, while at the same time applying the topical agent under evaluation.

Second, even the most common symptoms are very difficult to evaluate. One of the most frequent is itching; not only is the aetiology of itching unknown (1), but differences in severity can be noted both between patients and even in the same patient at different times, depending on such factors as time of day, state of emotion or the use of other drugs of which the doctor is unaware. Finally, it should be remembered that itching can persist even after the skin condition is clinically cured.

Thirdly, evaluation of a topical agent can be complicated by such factors as the addition of antibacterial substances, which although they are clinically indicated may tend to confuse the picture by producing sensitization reactions. Perhaps the commonest example is neomycin. This is said to cause less sensitization than other antibacterial agents and certainly *Friedrich* (2) has rarely seen neomycin sensitization. *Vermeulen & Malten* (8) have observed in a few cases a polyvalent sensitivity to neomycin and *Simons* (7) states that neomycin does cause sensitization but that this is often masked by the corti-

costeroid with which it is combined. Indeed, it may be said that if a skin condition under treatment with a corticosteroid and neomycin combined does not respond in the expected manner, it should always be considered whether or not there is 'masked' underlying irritation provoked by the neomycin. The author has himself observed sensitivity reactions to neomycin on several occasions, mostly in younger persons. The overall feeling is that corticosteroids should be given without neomycin, unless there is a specific indication.

A final point to consider in the evaluation of a topical skin preparation is the question of patient acceptability in relation to the form in which the drug is presented. *Krebs & Kuske* (3) state that most patients prefer a cream. Simons, however, found that 50 per cent of patients prefer an ointment, while only 15 per cent prefer a cream. In general an ointment will be prescribed for dry eczemas to aid skin elasticity and thus avoid cracking. Where the skin is naturally greasy a cream will often be most satisfactory, for example in seborrhoes. Lotions, being easily spread aqueous emulsions, are accordingly more suitable for acutely injured areas of skin such as occur in burning by ultra violet rays or perhaps in pruritis and other conditions affecting hairy skin. The foam preparation is again easily spread and is suitable for the treatment of acute lesions covering larger areas.

METHOD OF STUDY

A comparative investigation of Locacorten was performed by applying one or other of the various forms at the same time to contralateral body surfaces. The criteria for improvement were both objective as judged by decrease of exudation and, sometimes, of secondary infection, and subjective, as judged by decrease of itching and of the feeling of tension in the skin.

RESULTS

In assessing the degree of success an arbitrary scoring system was employed thus:

++ = Locacorten gives an excellent effect and there is no recurrence within 6 weeks.

+ = Locacorten gives good improvement within two weeks and is clearly superior to other topical corticosteroids.

± = Locacorten gives moderate improvement within one month and is no better than other steroids.

— = Locacorten gives no improvement, or certain symptoms are aggravated, or other steroid compounds have a better effect.

Key: o = ointment

c = cream

o+n = ointment with neomycin

c+n = cream with neomycin

l = lotion

s = spray

Condition	Res- ponse	Treatment						Totals
		o	o+n	c	c+n	l	s	
1. <i>Constitutional Eczema</i> (29 patients)	++	1	1	2	—	—	1	5
	+	6	—	8	2	1	3	20
	±	3	—	2	3	—	3	11
	—	1	—	1	1	2	1	6
2. <i>Neurodermatitis</i> (24 patients)	++	3	2	4	1	—	1	11
	+	7	4	3	1	—	—	15
	±	2	1	5	1	—	1	10
	—	2	—	2	1	1	—	6
3. <i>Contact Eczema</i> (13 patients)	++	—	2	2	—	1	1	6
	+	3	—	2	—	—	—	5
	±	1	1	2	2	2	—	8
	—	—	—	1	2	1	2	6
4. <i>Dyshidrotic Eczema</i> (14 patients)	++	1	1	—	2	2	—	6
	+	2	2	2	1	1	—	8
	±	2	—	2	2	—	—	6
	—	1	2	1	—	—	2	6
5. <i>Drug Eczema</i> (9 patients)	++	—	—	—	—	2	—	2
	+	2	—	3	2	—	1	8
	±	—	1	—	—	1	—	2
	—	1	—	1	—	—	—	2

Condition	Res- ponse	Treatment						Totals
		o	o+n	c	c+n	l	s	
6. <i>Various Eczemas</i> (head + neck) (16 patients)	++	-	-	1	-	1	2	4
	+	-	-	2	-	6	3	11
	±	-	-	1	1	1	-	3
	-	-	1	-	1	-	-	2
7. <i>Various Eczemas</i> (trunk and limbs) (12 patients)	++	-	1	-	-	1	-	2
	+	1	2	-	1	2	-	6
	±	-	1	-	2	-	1	4
	-	-	-	1	1	1	1	4
8. <i>Ichthyosis</i> (5 patients)	++	-	-	-	-	-	-	-
	+	1	1	-	-	-	-	2
	±	1	-	2	1	-	2	6
	-	-	1	-	-	1	-	2
9. <i>Ultra-violet Light</i> <i>Dermatitis</i> (5 patients)	++	-	-	-	-	1	1	2
	+	-	-	-	-	3	2	5
	±	-	-	1	-	-	1	2
	-	1	-	-	-	-	-	1
10. <i>Urticarial Eczema</i> (9 patients)	++	1	-	1	-	1	-	3
	+	-	-	1	1	2	1	5
	±	1	-	1	-	1	1	4
	-	1	-	-	1	1	1	4
11. <i>Psoriasiform Eczema</i> (5 patients)	++	-	-	-	-	-	1	1
	+	-	3	1	-	-	1	5
	±	-	-	1	-	-	-	1
	-	-	-	-	-	1	-	1
12. <i>Impetigo</i> (2 patients)	++	-	1	-	1	-	-	2
	+							-
	±							-
	-							-
13. <i>Pityriasis Capitis</i> (3 patients)	++	-	-	-	-	-	-	-
	+	-	-	-	-	1	-	1
	±	-	-	-	-	1	1	2
	-	-	-	-	-	1	-	1

DISCUSSION

All the patients, with the exception of those with impetigo, those with light sensitive dermatitis and a few of those with drug induced eczema, had previously been treated with other products, largely without success. In a number of the cases where Locacorten had been used successfully it was compared with various other cortiosteroid preparations.

A hydrocortisone ointment was without effect in twenty instances and gave results inferior in six and superior in two cases compared with Locacorten.

There was a further thirty-seven cases where virtually no results could be obtained with any other topical corticosteroids.

There were several failures with Locacorten:

One asthmatic patient on prednisolone developed a drug eczema which was unaffected by Locacorten.

One patient with photosensitivity experienced acute burning and stinging with Locacorten ointment and had to abandon treatment.

With preparations containing added neomycin there were four instances of severe irritation.

A few patients, mostly men, suffered excessive drying of the skin after using the lotion or foam and in some cases this proceeded to fissuring in the interdigital clefts. Finally, one patient with eczema failed to respond to Locacorten, possibly due to hormonal factors since it was later found that she had an ovarian cyst and multiple cysts of the breast.

Summing up, it may be said that Locacorten in its various forms gave highly satisfactory results. It is interesting in the light of this series of cases to examine the results of some other workers who have used Locacorten.

Weitgasser (4) had 25 failures among 192 patients.

Krebs & Kuske (3) quote 13 failures among 160 patients and

Friderich (2) obtained an unsatisfactory result in 7 per cent of his series.

SUMMARY

Compared with other steroid preparations for external application Locacorten may be regarded as an important acquisition to our therapeutic arsenal; a principal advantage is the low steroid percentage, made possible by the doubly-fluorinated compound, so that the number of unwanted effects is small. Such undesirable effects as have been observed may sometimes have been due to the addition of neomycin. Both the ointment and the cream are also commercially available without the addition of neomycin. Compared with other steroid preparations for external application, the price of this product is not high.

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