COMPARATIVE INVESTIGATION WITH FLUPREDNYLIDENE ACETATE (DECODERM)

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Summary

The therapeutic efficacy of a new fluorinated steroid, 0.1% fluprednylidene-21-acetate (Decoderm) cream was compared to betamethasone and triamcinolone in two double blind clinical trials. All the three topical steroids were effective in various steroid responsive dermatoses within one week and the beneficial effects continued throughout the four weeks of the trials. The various signs and symptoms, such as erythema, pruritus, oedema, exudation, scaling, vesicles, crusting, lichenification and burning, improved significantly with each of the steroids under trial. Fluprednylidene-21-acetate (Decoderm) cream represents an important addition to the presently available topical steroids.

The wide use of topical steroids in the treatment of inflammatory skin diseases now encompasses more potent preparations such as triamcinolone, betamethasone and the newer fluorinated steroids. Recent work with a new fluorinated steroid, fluprednylidene-21-acetate (9 ∝-fluoro-16 methyleneprednisolone-21-acetate) has demonstrated a high therapeutic effieacy with practically no notable side effects. We have reported earlier the excellent therapeutic efficacy of fluprednylidene - 21 - acetate (Decoderm) cream in steroid responsive dermatoses[1] and the absence of any significant effect on plasma cortisol levels in patients treated with percutaneous application of Decoderm cream[2]. On the basis of these findings, we decided to undertake two separate double blind studies to compare Decoderm with betamethasone and triamcinolone.

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Methods

Eighty patients participated in the two double blind clinical trials carried out to assess the relative efficacy of Decoderm as compared to triamcinolone (study A) and betamethasone (study B). Forty-five of these patients including 33 males and 12 females of the age ranging from 11 to 72 years, participated in study A whereas 35 patients including 21 males and 14 females of the age range of 19 to 75 years, participated in study B. All the patients selected for the trials had bilateral skin diseases mentioned in table 1, of approximately the same extent and severity, on both the right and left sides of the body so as to allow comparison of two different medications on two different sides (right and left) of the body.

Each of the two trials, study A and study B, was a double blind comparative study of two topical steroid preparations. All previous topical therapy on the affected areas was stopped at

least one week prior to the study. Each patient was examined clinically and assessed as regards the morphological subsidence of the lesions, erythema, pruritus, oedema, exudation, scaling, vesicles, crusting, lichenification, nodules and burning, before the trial was started. Each of these signs/symptoms was graded on a score of 0 = absent, ± = 1, + = 2, ++ = 3, +++ = 4, ++++ = 5, so that the maximum score at the pretreatment stage for any patient could have been 50.

Each patient was given two types of medication tubes (Decoderm and triamcinolone in study A, and Decoderm and betamethasone in study B) of two different colours and each marked with a code number and a letter 'R' or 'L' indicating the side of the body (right or left) to which the medication was to be applied. The medication marked either 'R' or 'L' varied according to the code number in order to exclude bias.

Patients were asked to apply twice daily for four weeks the creams using two tubes marked for right (R) and left (L) sides of the body, and report at weekly intervals. Each patient was examined weekly for four weeks to grade the same signs and symptoms as for the pretreatment assessment and to note side effects if any. On conclusion of the four weeks' trial, the codes were opened and the details in the trial proformas were assessed.

The total score was calculated for each patient taking into consideration all the signs/symptoms graded at the pretreatment stage and at weekly intervals during the trial. Reduction in the total score brought about by each medication was calculated for weekly intervals in order to note the improvement. The data was analysed by means of the students 't' test. Similarly, improvement in individual sign/symptom with each medication was calculated by the students 't' test.

TABLE 1

Clinical Condition	Number of Patients	
	Study A	Study B
1. Contact dermatitis	26	21
2. Constitutional eczema :		
(i) Neurodermatitis	3	1
(ii) Atopic dermatitis	5	4
(iii) Nummular dermatitis	3	—
(iv) Xerotic dermatitis	2	3
(v) Infectious eczematoid dermatitis	2	1
(vi) Seborrhoeic dermatitis	—	3
3. Stasis eczema	4	2
Total	45	35

Results

The data on reduction in the total score calculated from the grading of various signs and symptoms at each weekly interval for four weeks of the trials A and B, is presented in tables 2 and 3.

From these results it is clear that all the three medications tried in the two double-blind trials were highly effective ($p < 0.001$). Significant activity was seen within the first week of commencement of therapy and the improvement brought about by the three medications, continued throughout the trial period.

Improvement in the individual sign or symptom brought about by various medications in the two clinical trials is presented in table 4.

All the signs and symptoms, except the nodules, improved significantly ($p < 0.001$) with the use of the three medications under trial. There was no significant difference in the efficacy between Decoderm and betamethasone or Decoderm and triamcinolone.

No side effects were noted during the trial with any of the three medications.

TABLE 2
Improvement brought about at weekly intervals by Decoderm and triamcinolone in study A

Treatment Group	Difference in total score (Mean ± SEM) at the end of			
	1st Week	2nd Week	3rd Week	4th Week
Triamcinolone	8.77 ± 0.89*	12.98 ± 1.13*	15.5 ± 1.42*	15.8± 1.51*
Decoderm	8.56 ± 1.39*	12.37 ± 1.22*	13.67 ± 1.4*	14.06 ± 1.53*
Comparison of the two groups	NS	NS	NS	NS

*=$p < 0.001$ NS=Nonsignificant ($p > 0.1$)

TABLE 3
Improvement brought about at weekly intervals by Decoderm and betamethasone in study B

Treatment Group	Difference in total score (Mean ± SEM) at the end of			
	1st Week	2nd Week	3rd Week	4th Week
Betamethasone	8.18 ± 1.14*	12.0 ± 1.28*	13.47 ± 1.47*	13.77±1.02*
Decoderm	8.74 ± 1.15*	11.34 ± 1.19*	13.63 ± 1.56*	13.5 ± 1.55
Comparison of the two treatment groups	NS	NS	NS	NS

*=$p < 0.001$ NS=Nonsignificant ($p > 0.1$)

Discussion

The data obtained in these trials has confirmed the excellent therapeutic efficacy of Decoderm cream which was observed by us in our open trial with the cream earlier[1] and by several other authors, such as Garretts[3], Freshwater[4], Lundell[5], Weitgasser[6], Serra[7], Koves de Amini[8], Landes et al[9], Schreiner[10] and Schwind[11]. It must be noted that Decoderm cream is effective both in dry and moist skin lesions.

In these two trials, Decoderm cream and the other two steroids betamethasone and triamcinolone were equally effective in various dermatological disorders, such as contact dermatitis, constitutional eczema (neurodermatitis, atopic dermatitis, nummular dermatitis, xerotic dermatitis, infectious eczematoid, seborrhoeic dermatitis) and stasis eczema.

It is evident from table Nos. 2 and 3 that the total score was reduced significantly ($p < 0.001$) by all the three topical medications tested in the two studies. Similarly, the improvement in various signs or symptoms (table No. 4) brought about by the three medications had the same statistical significance ($p < 0.001$). Since the level of significance is high ($p < 0.001$) on parametric analysis, it must be noted that the finer differences in the response to treatment with various therapies cannot be demonstrated objectively.

Decoderm cream, however, had certain cosmetic advantages over the other two medications in that it was more acceptable to the patients since it was easy to apply and did not soil the underclothing. This is mainly because of its cream base which in contrast to the conventional oil-in-water and water-in-oil emulsions, is a mixed emulsion with a complete uniform distribution of the two phases[12]. Thus unique formulation of the cream base gives it the capacity to take up large quantities of

TABLE 4

Improvement in signs / symptoms brought about by various medications in study A and study B

Study	Treatment Group	Sign / symptom score-difference between pre-treatment score and score after four weeks									
		Eryrhema	Pruritus	Oedema	Exudation	Scaling	Vesicles	Crusting	Licheni-fication	Nodules	Burning
A	Triamcinolone	1.41±0.21*	2.91±0.24*	1.56±0.26*	1.47±0.26*	1.91±0.24*	1.68±0.25*	1.78±0.22*	1.63±0.24*	0.28±0.15	1.22±0.26*
	Decoderm	1.34±0.22*	3.06±0.26*	1.41±0.24*	1.25±0.23*	1.41±0.24*	1.47±0.25*	1.38±0.23*	1.53±0.25*	0.22±0.12	1.13±0.25*
	Camparison of triamcinolone and Decoderm	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
B	Betamethasone	1.35±0.27*	2.73±0.24*	1.00±0.25*	1.00±0.23*	1.38±0.25*	0.88±0.25*	1.12±0.27*	2.04±0.18*	0.04±0.4	1.62±0.33*
	Decoderm	1.35±0.3*	2.58±0.12*	1.07±0.25*	0.96±0.27*	1.58±0.25*	0.96±0.26*	1.31±0.28*	2.12±0.23*	0.08±0.05	1.65±0.34*
	Comparison of betamethasone and Decoderm	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

*=$p < 0.001$ NS=Nonsignificant ($p > 0.1$)

both oil and water without losing its stability.

Decoderm cream has a remarkable advantage due to its penetration kinetics in the skin. It penetrates rapidly into the skin immediately after application. The maximum penetration rate of the steroid was found to occur in the first hour of its application[13]. After initial rapid penetration, fluprednylidene-21-acetate accumulates at a barrier in the epidermis and forms a depot for protracted release thereafter. Experiments on human skin using the techniques of skin sectioning[14] and autoradiography[13,15], demonstrated that the barrier for Decoderm cream was limited to the stratum corneum. The peculiar penetration kinetics of Decoderm provide three important advantages: lack of systemic side effects, absence of local side effects and prolonged duration of therapeutic action. Decoderm cream does not affect the formation of collagen since the penetration of the corticoid into the collagen synthesising layers is delayed due to the depot effect. Milbradt[16] observed in his double-blind clinical trial that therapeutic improvement was obtained with even once daily application of Decoderm cream. Freshwater[4] confirmed the finding of Milbradt[16] and concluded that a single application of fluprednylidene-21-acetate cream was sufficient for therapeutic efficacy and the success obtainted with this treatment could not be significantly exceeded by a thrice daily application of the cream.

Decoderm cream, therefore, in due consideration to the therapeutic efficacy in steroid responsive dermatoses, absence of effect on plasma cortisol levels[2] and the excellent local and systemic tolerance, represents an important addition to the presently available topical steroids.

Conclusion

We feel that the new fluorinated steroid, fluprednylidene-21-acetate (Decodem) cream is equally effective in steroid responsive dermatoses as compared to betamethasone and triamcinolone. The morphological subsidence of lesions and relief from various signs and symptoms were brought about within one week. Fluprednylidene-21-acetate (Decoderm) cream, however, had an added advantage since it did not soil the underclothing.

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