

Pharmacology and Treatment

Br. J. Derm (1968) **80**, 614.

I.C.I. Pharmaceuticals, Alderley Park, Cheshire.

FLUOCINOLONE ACETONIDE 0.2% CREAM— A CO-OPERATIVE CLINICAL TRIAL*

C. W. MARSDEN

SUMMARY.—The response to a 0.2% fluocinolone acetonide cream is reported in 192 patients with a variety of skin conditions. Results were particularly successful in chronic discoid lupus erythematosus, necrobiosis lipoidica, lichen planus and granuloma annulare. Some cases of pustular psoriasis of the palms and of keloids responded well. Occasional benefit occurred in mycosis fungoides and in pemphigus erythematosus but in general the results in these last 2 conditions were disappointing. No serious adverse effects were seen in this series.

To publish another paper on the use of topical corticosteroids might seem superfluous. To do so demands that the corticosteroid should be either cheaper, safer, or more effective in responsive conditions or that it should increase the range of diseases in which topical corticosteroids are effective. This paper is concerned merely with this last advantage.

In 1964, Tye, *et al.*, described the beneficial results in a case of pemphigus erythematosus treated with 0.2% fluocinolone acetonide cream. At that time some response was also reported in pretibial myxoedema by Kriss *et al.* (1964) and in a case of granulomatous hypersensitivity by Epstein and Allen (1964). Further good results in pemphigus erythematosus have been reported by Baer *et al.* (1966) and by Orfuss *et al.* (1966) and in pretibial myxoedema by Shasky and Nelson (1966) and Kriss *et al.* (1967).

Other writers have reported benefit in mycosis fungoides (Farber *et al.*, 1966; Tuffanelli, 1966) and in epidermolysis bullosa (Severin and Farber, 1967). Imperato and Callaway (1967) reported their findings in a variety of conditions, chronic discoid lupus erythematosus, granuloma annulare, necrobiosis lipoidica, keloids and single cases of hypertrophic lichen planus, lymphocytoma and polymorphous light eruption.

MATERIALS AND METHODS

The present series comprises 192 patients with a variety of skin conditions, who received treatment with 0.2% fluocinolone acetonide in a cream base. The cream was applied 3 times daily, without occlusion, by the majority. Occlusion was

Accepted for publication March 21st, 1968.

* The following clinicians carried out this study:

Dr. J. G. Coburn, Manchester; Professor S. Jablonska, Warsaw; Dr. P. E. Kilby, Derby; Dr. J. A. Leeming, Johannesburg; Dr. R. M. B. MacKenna, London; Dr. P. C. Mitchell, Carlisle; Dr. B. Portnoy, Manchester; Dr. P. D. Samman, London; Dr. I. Sarkany, London; Dr. C. F. H. Vickers, Liverpool.

C. W. MARSDEN



22. 5. 67.



22. 6. 67.

Epidermolysis Bullosa (Dr. J. A. L. Leeming)



8. 9. 67.



18. 10. 67.

Lichen Planus Verrucosus (Dr. J. A. L. Leeming)

FLUOCINOLONE ACETONIDE 0.2% CREAM



20. 6. 67.



15. 8. 67.

Chronic Discoid Lupus Erythematosus (Dr. B. Portnoy)



20. 10. 66.



27. 10. 67.

Necrobiosis Lipoidica (Dr. I. Sarkany)

used in a few patients, for example those with necrobiosis lipoidica. Skin disease had been present in most patients for years and previous treatments had included a variety of topical corticosteroids besides other therapy.

The results were recorded on a standard reporting form and a summary of the diseases together with the response achieved is given in the table. Photographs before and after treatment show the results in four representative conditions.

TABLE I.—*Response to Treatment with 0.2% Fluocinolone Acetonide Cream in Various Skin Disorders*

Diagnosis	Clear	Significant Response	Poor or no response	Worse	Comment	Total
Lupus erythematosus (Chronic Discoid)	20	49	6	1	2 cases were regarded as showing signs of systemic type	76
Necrobiosis Lipoidica	4	13	1	—	4 cases with occlusion at night	18
Reticuloses						
Mycosis Fungoides	2	4	6	1		13
Other types	1	—	2	—	temporary response in parapsoriasis	3
Psoriasis						
Pustular Palms	3	7	5	—		15
Other types	1	4	1	—		6
Keloids	2	7	3	—		12
Granuloma annulare	1	5	1	—		7
Bullous eruptions						
Pemphigus Erythematosus	1	1	1	1		4
Dermatitis Herpetiformis	—	—	5	—	adult type	5
Epidermolysis Bullosa	—	2	—	—	dystrophic type	2
Resistant eczema, pruritus ani and prurigo	4	7	2	—	failures: chronic eczema of palms 1, prurigo nodularis 1	13
Lichen planus verrucosus	2	4	1	—		7
Miscellaneous	2	2	7	—	see text	11
Total	43	105	41	3		192

DISCUSSION

The largest series of cases treated was lupus erythematosus (76 patients) and these can be considered in greater detail. Duration of the disease was between 6 months and 37 years with an average of 9.3 years. Over 60% (62.0%) had already been treated with topical corticosteroids, 20% (19.7%) with occlusion. Eight cases (11.25%) had previously received treatment by intralesional injection of corticosteroids, a method recommended for long-standing cases persisting after treatment with antimalarials (Rowell, 1962). Sixty per cent (59.2%) had received antimalarials, leading in 2 cases to retinopathy. The results in this condition were impressive; several clinicians noted that after a significant response to the 0.2% cream many cases could be maintained with fluocinolone acetonide at the usual 0.025% concentration.

Particular care is necessary in assessing the results in mycosis fungoides. Any response in the skin manifestations is unlikely to be more than temporary. In this series the disease had been present for from 3–30 years (average 15.7 years).

Six of the 13 patients had received topical corticosteroids previously and 8 had been treated with electron beam or radio-therapy. Although 2 patients showed a dramatic response the overall picture was less encouraging than that reported by previous authors (Farber *et al.*, 1966; Tuffanelli, 1966).

Very great improvement, in some cases the clearing of all active lesions leaving only scarring or pigmentation, was seen in necrobiosis lipoidica and in lichen planus verrucosus. Although granuloma annulare may often remit without obvious cause the condition had been present in some patients for years without changing clinically.

In pustular psoriasis of the palms and in keloids the response was variable. Some patients improved markedly or even cleared whilst others failed to respond. The reasons for this variation are not obvious.

The results in bullous diseases are interesting. Success in pemphigus erythematosus has been reported by a number of authors (Tye *et al.*, 1964; Baer *et al.*, 1966; Orfuss *et al.*, 1966). In our series a satisfactory response was seen in 2 cases with failure in 2 others. Two cases of dystrophic epidermolysis bullosa, a brother and sister, showed considerable benefit. This has also been reported by Severin and Farber (1967). Dermatitis herpetiformis in 5 patients was not relieved.

The material was also applied to a miscellaneous group of conditions. One case of polymorphous light eruption and one of Darier's Disease benefitted. A poor result was recorded in single cases of annular sarcoidosis, pretibial myxoedema, morphea and alopecia areata.

SIDE EFFECTS

No important side effects were seen. Single patients complained of pain, itching and burning after application of the cream. One patient (long-standing chronic discoid lupus erythematosus) developed superficial ulceration which healed rapidly on changing to 0.025% fluocinolone acetonide cream. Two cases of folliculitis were reported. In this series no atrophic striae were observed although there is no reason to suppose that this may not occasionally occur as with other powerful topical corticosteroids. Topical steroids should, of course, always be prescribed in the lowest effective concentration.

There was no clinical evidence of systemic absorption. Biochemical studies were not made in this series but have been carried out in America (personal communication, Syntex Laboratories, Palo Alto, California). Using the measurement of 17-oxosteroids by the method of Dreker (1952) with modification by Sobel (1958) and Golub (1958) and the 17-oxogenic steroids by either the method of Sobel (1958) and Golub (1958) or that of Rutherford and Nelson (1963) in 6 adults with continuous occlusion for periods of over 12 hr. no significant change in adrenal function was seen with amounts ranging from 1-3 G. cream daily in 4 patients with psoriasis vulgaris and with 5 G. daily in 2 normal subjects.

It is impossible to name all those members of the various hospital staffs who assisted with this study. In particular, however, we would like to thank the patients for their helpful co-operation.

REFERENCES

- BAER, R. L., ANDRADE, R. and SELMANOWITZ V. J. (1966) Pemphigus Erythematosus. *Archs Derm.*, **93**, 374.
- DREKTER, I. J., HESLER, A., SCISM, G. R., STERN, S., PEARSON, S. and MCGAVACK, T. H. (1952) The Determination of Urinary Steroids. I. The Preparation of Pigment Free Extracts and a Simplified Procedure for the Estimation of Total 17-Ketosteroids. *J. clin. Endocr. Metab.*, **12**, 55.

- EPSTEIN, W. L. and ALLEN, J. R. (1964) Granulomatous Hypersensitivity After Use of Zirconium-Containing Poison Oak Lotions. *J. Am. med. Ass.*, **190**, 940.
- FARBER, E. M., COX, A. J., STEINBERG, J. and McCLINTOCK, R. P. (1966). Therapy of Mycosis Fungoides with Topically Applied Fluocinolone Acetonide Under Occlusive Dressing. *Cancer N. Y.*, **19**, 237.
- GOLUB, O. J., SOBEL, C. and HENRY, R. J. (1958) Comparative Study of the 17-Ketogenic (Norymberski), Glenn-Nelson and Reddy Methods for the Determination of C₂₁ Urinary Steroids. *J. clin. Endocr. Metab.*, **18**, 522.
- IMPERATO, P. J. and CALLAWAY, J. L. (1967) High Concentration Fluocinolone Cream in the Management of Resistant Dermatoses. *N. Carol. med. J.*, **28**, 276.
- KRISS, J. P., PLESHAKOV, V. and CHIEN, J. R. (1964) Isolation and Identification of the Long-Acting Thyroid Stimulator and its Relation to Hyperthyroidism and Circumscribed Pretibial Myxedema. *J. clin. Endocr. Metab.*, **24**, 1005.
- KRISS, J. P., PLESHAKOV, V., ROSENBLUM A. and SHARP, G. (1967) Therapy with Occlusive Dressings of Pretibial Myxedema with Fluocinolone Acetonide. *J. clin. Endocr. Metab.*, **27**, 595.
- ORFUSS, A., ANDRADE, R. and PETRATOS, M. (1966) Pemphigus Erythematodes in a Child. *Archs Derm.*, **94**, 524.
- ROWELL, N. R. (1962) Treatment of Chronic Discoid Lupus Erythematosus with Intralesional Triamcinolone. *Br. J. Derm.*, **74**, 354.
- RUTHERFORD, E. R. and NELSON, D. H. (1963) Determination of Urinary 17-Ketogenic Steroids by Means of Sodium Metaperiodate Oxidation. *J. clin. Endocr. Metab.*, **23**, 533.
- SEVERIN, G. L. and FARBER, E. M. (1967) The Management of Epidermolysis Bullosa in Children. *Archs Derm.*, **95**, 302.
- SHASKY, D. and NELSON, J. (1966) Pretibial Myxedema. *Archs Derm.*, **94**, 658.
- SOBEL, C., GOLUB, O. J., HENRY, R. J., JACOBS, S. L. and BASU, G. K. (1958) Study of the Norymberski Methods for Determination of 17-Ketogenic Steroids (17-hydroxycorticosteroids) in Urine. *J. clin. Endocr. Metab.*, **18**, 208.
- TUFFANELLI, D. L. (1966) Mycosis Fungoides. *Archs Derm.*, **94**, 250.
- TYE, M. J., BLUMENTAL, G. and LEVER, W. F., (1964) Pemphigus Erythematosus. *Archs Derm.*, **90**, 307.
-
-

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.