PLASMA CORTISOL LEVELS AFTER TOPICAL USE OF FLUOCINOLONE ACETONIDE.

LIONEL FRY, B.Sc., M.D., M.R.C.P.,*
Registrar, Skin Department,
AND
D. G. D. WIGHT, M.B., B.CHIR.
Resident Pathologist, St. Thomas' Hospital, London, S.E.1.

EVIDENCE of suppression of the adrenal cortical hormones by topical steroids used under polythene occlusive dressings in the treatment of psoriasis has recently been reported by Scoggins (1962), Gill and Baxter (1964) and Kirketerp (1964). Scoggins and Kirketerp used fluocinolone acetonide 0·025% and Gill and Baxter 0·01%.

Scoggins, Gill and Baxter only studied subjects who had had " total body occlusion " using 45 g. or more of the cream. Scoggins applied this quantity of cream twice daily and Gill and Baxter only once a day followed by a 12-hour period of occlusion. Kirketerp occluded 17–78 % of the skin and applied 10 g. of the cream daily to each 17% of body surface occluded. Even using as little as 10 g. of cream, Kirketerp found a decrease in the urinary excretion of the 17-ketogenic steroids.

In practice it has been found that the clinical results of treatment with weaker concentrations of fluocinolone acetonide than those of the standard (0·025 and 0·01%) commercial preparations are satisfactory. Further, occlusion of the entire skin surface is not as frequently employed as occlusion of smaller areas. This form of therapy is now employed extensively as outpatient treatment, and in some instances for a considerable length of time. We have studied the effect of the use of a weak preparation of fluocinolone acetonide in such cases in order to determine whether suppression of the plasma 11-hydroxy-corticosteroids (plasma cortisol) occurs.

Investigations by Christy *et al.* (1956) suggested that small doses of oral steroids administered for a long time (i.e. 6–12 months) may be more likely to suppress adrenal cortical function in conditions of stress than larger doses of oral steroids for a short time (i.e. approximately 1–4 weeks). Thus protracted occlusive therapy with topical steroids, might prove a hazard to the patient.

INVESTIGATION.

Six healthy subjects who received no applications of steroids were investigated to see if there was daily fluctuation of the plasma cortisol levels. Blood for plasma cortisol estimations was taken at 10 a.m. on at least three consecutive days.

* Present address : The London Hospital, London, E.1.

Eighteen patients were studied: 11 had psoriasis, 6 eczema and 1 lichen planus. Fluocinolone acetonide 0·0062% in an ointment base was used. Five g. of the ointment (0·31 mg. of fluocinolone) was applied to the lesions each day at 7 p.m. and if there was excess of ointment after applying it to the lesions it was applied to the normal skin surrounding them. The limb or limbs, and in one instance the trunk, were then covered with occlusive plastic dressings which were left in position for 12 hours. The procedure was repeated daily for a total of 7 days. In no instance was more than 5 g. required to cover the lesions in the area to be occluded. In a number of patients lesions were present at other sites which were not treated.

Blood for plasma cortisol estimations was taken at 10 a.m. on the day that treatment was due to be started, after 7 days of treatment and 7 days later. During this latter period the patients received no other treatment. Plasma cortisol was estimated by the method described by Mattingly (1962). The clinical response to treatment was graded as worse (−), no change (0), moderate improvement (+), and marked improvement (++).

Results

All the patients studied showed some clinical improvement after the treatment period (Table I). It was moderate in 4 and marked in 14.

Table I.—*Clinical Features and Plasma Cortisol Levels of the Subjects Investigated.*

Case.	Age.	Sex.	Diagnosis.	Area of body occluded.	Area of diseased skin in occluded site (%).	Clinical response.	Plasma cortisol (μg./100 ml.)		
							Before treatment.	After treatment.	7 days after stopping treatment.
1	45	M	Psoriasis	Arms and legs	30	+	14	10	10
2	26	F	,,	,,	30	++	16	14	17
3	29	M	,,	Legs	25	+	11	9	10
4	24	F.	,,	Trunk	50	++	7	9	7
5	38	F	,,	Legs	20	+	13	13	17
6	41	F	,,	,,	30	++	10	8	12
7	56	M	,,	,,	20	++	8	12	—
8	40	F	,,	Arms	40	++	11	12	13
9	25	F	,,	,,	15	++	10	11	31
10	26	F	,,	Legs	30	++	12	14	12
11	21	F	,,	,,	10	+	6	7	—
12	45	F	Eczema	Arms	20	++	12	8	12
13	65	M	,,	,,	50	++	19	13	14
14	60	M	,,	,,	20	++	14	13	13
15	42	M	,,	One leg	30	++	16	15	16
16	16	F	,,	Arms	20	++	15	16	19
17	42	M	,,	One leg	30	++	24	19	12
18	24	M	Lichen planus	Legs	10	+	25	19	11

There was no significant difference in cortisol levels measured in the control subjects measured on three consecutive days (Table II) or between them and the three estimations of plasma cortisol levels in the patients (Table I).

There was no significant fall in the plasma cortisol levels in any patients after treatment (Table I); there was a fall in 10, a rise in 7, and in one there was no change. The plasma cortisol levels before and after treatment, in the patients as a group, do not differ ($P>0·010$).

The clinical improvement in the skin disease was not related to a rise or fall in the plasma cortisol level after treatment. There was no relationship between the area occluded, the area of diseased skin in the occluded site and the subsequent plasma cortisol levels. No significant difference was noted between the plasma cortisol levels in the patients with psoriasis and those with eczema.

TABLE II.—*Plasma Cortisol (μg./100 ml.) in Control Subjects on Consecutive Days.*

Subject No.	Day 1	2	3	4
1	23	22	11	14
2	10	17	14	12
3	9	7	10	9
4	10	9	11	10
5	15	12	16	—
6	11	12	18	—

When the plasma cortisol levels after the 7-day treatment period are compared with the plasma cortisol levels after the patients had stopped treatment for 7 days there is found to be no significant differences ($P>0{\cdot}20$). This tends to confirm that there has been no suppression of cortisol levels due to treatment.

DISCUSSION.

In this investigation no significant suppression of plasma cortisol levels was found in patients with psoriasis, eczema or lichen planus when treated with fluocinolone acetonide under polythene occlusive dressings in the regime described above. This regime was sufficient to produce considerable clinical improvement. Plasma cortisol levels were chosen as an index of the activity of the pituitary–adrenal axis as Gill and Baxter (1964) reported this to be a more reliable test than the 24-hour urinary excretion of 17-ketosteroids and 17-hydroxycorticosteroids.

If suppression of adrenal cortical hormones (or their products) does occur it becomes evident within twenty-four hours of starting treatment, and begins to return to pre-treatment levels within two days of stopping treatment. (Scoggins, 1962 ; Gill and Baxter, 1964 ; Kirketerp, 1964). Thus the limits of time chosen in this study seemed to be adequate to detect significant changes in the plasma cortisol. In the previous reports far greater quantities of fluocinolone acetonide were used for twenty-four hour periods than those used in this study. Scoggins (1962) used 30 mg. and 22·5 mg. of fluocinolone acetonide in two patients respectively, Gill and Baxter (1964) used 4·5 mg. in their patients, and Kirketerp (1964) used a range of 2·5–10·0 mg. It is probable therefore that in the dosage and scheme employed in this study the amount of steroid absorbed was not great enough to suppress the pituitary-adrenal axis.

The suppression of plasma cortisol following the use of topical steroids is not peculiar to fluocinolone acetonide. Gill and Baxter (1964) reported it after the use of triamcinolone acetonide and flurandrenolone acetonide. They did however report a difference in response to treatment between normal subjects, patients with alopecia universalis, and in patients with psoriasis. They found suppression of plasma cortisol only in the patients with psoriasis.

It seems probable, therefore, that fluocinolone acetonide and probably the other new topical steroids can be used under polythene occlusive dressings without causing suppression of the plasma cortisol level, if the total amount of steroid employed in a twenty-four hour period is below a certain quantitiy. This quantity appears to be sufficient to achieve a satisfactory clinical response, according to the results obtained in this study. Further studies are required to find the amount of topical steroid that can be used without causing suppression of the pituitary-adrenal axis, and this quantity may vary for different diseases. It would be possible to decrease the total quantity of steroid used either by using weaker concentrations than those employed in the proprietary preparations (but of a sufficient concentration to give a good clinical response), or if there is widespread disease, by not occluding more than a certain area of the body surface at a time.

Finally, it should be mentioned that a fall in the plasma cortisol levels may not be the most sensitive or the most appropriate test for measuring the failure of the pituitary-adrenal axis to respond to " stress " ; and further elucidation of this point is required.

Summary.

Plasma cortisol levels have been estimated before and after treatment with topial fluocinolone acetonide under polythene occlusive dressings. Eleven patients with eczema, six with psoriasis and one with lichen planus were included in this investigation. Using 0·0062% fluocinolone acetonide and not occluding more than half the total body surface, no significant suppression of plasma cortisol was found after treatment. All subjects studied showed a clinical improvement in their skin disease.

Further studies are required to determine the quantity of the newer topical steroids that can be applied under polythene occlusive dressings without causing suppression of the pituitary-adrenal axis.

We wish to thank Dr. H. J. Wallace for his encouragement and for allowing us to study patients under his care, and Dr. R. R. McSwiney for his advice and for providing laboratory facilities.

References.

Christy, N. P., Wallace, E. Z. and Jailer, E. W. (1956) *J. clin. Endocrin.*, **16**, 1059.
Gill, K. A. and Baxter, D. L. (1964) *Arch. Derm.*, **89**, 734.
Kirketerp, M. (1964) *Acta derm-venereol., Stockh.*, **44**, 54.
Mattingly, D. (1962) *J. clin. Path.*, **15**, 374.
Scoggins, R. B. (1962) *J. invest. Derm.*, **39**, 473.