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The effect on plasma corticosteroid levels of the short term topical application of clobetasol propionate

STUART R.WALKER, LYN WILSON, LIONEL FRY AND V.H.T.JAMES

Clinical Research Unit, Glaxo Laboratories Ltd, Greenford, Middlesex, and East Ham Memorial Hospital and Department of Chemical Pathology, St Mary's Hospital, London, W.2

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SUMMARY

Thirty-four patients with skin diseases which necessitated treatment with potent topical steroids at a hospital clinic were studied. All the patients received clobetasol propionate ointment (Dermovate) for a period of 2 weeks and sixteen of the patients continued with their treatment for 4 weeks, during which time their plasma corticosteroid levels were measured. Thirty patients had normal levels throughout the whole period of study ($\geqslant$ 6 μg/100 ml) and five patients showed a depressed level at some stage during the investigation. Of six patients who were using a large amount of clobetasol ointment (more than 100 g/week) and who had a significant proportion of their body affected by disease (20–80%), two had lowered plasma corticosteroid levels and in four there was no evidence of adrenal suppression.

It has been shown previously that only a very small proportion of those patients being treated with topical steroids have plasma corticosteroid levels below normal (Fry & Wight, 1965; Wilson, Williams & Marsh, 1973; Munro & Clift, 1973). However, those topical steroids which are clinically effective can be absorbed through the skin when applied topically under occlusion to such an extent that depression of adrenocortical function occurs (James, Munro & Feiwel, 1967). Therefore the introduction of a new steroid warrants an investigation of this possibility in patients for whom it is being prescribed.

A new topically active corticosteroid, clobetasol propionate (Dermovate), has been investigated in double-blind comparative trials in several dermatological clinics and has been shown to be highly effective, especially in the treatment of psoriasis (Sparkes & Wilson, 1974).

The following study was designed to determine whether the topical application of clobetasol ointment (0·05%) in typical clinical situations has a detectable effect on plasma corticosteroid levels.

PATIENTS AND METHODS

Adult out-patients who would normally be treated with potent topical steroids were included in the study. However, the following patients were excluded: pregnant women, patients receiving systemic steroids (including oral contraceptive tablets), those who had received systemic steroids within the

previous 3 months and those whose treatment or disease was known to affect their hypothalamic–pituitary-adrenal function.

At the first interview the clinical details and diagnosis of each patient were recorded. An estimation was made of the total body area affected by the disease. The patients were carefully questioned about any drugs taken, including their topical steroid regimen. Details of the type of steroid, the amount used per week, the duration of use and whether or not occlusive dressings were employed, were recorded.

At the time of the interview venous blood (10 ml) was collected in a heparinized tube. This was later analysed for plasma corticosteroid levels using a fluorimetric assay (Townsend & James, 1968), and duplicate estimations were carried out on each of the samples. Blood was taken for plasma corticosteroid estimations between 10.00 and 12.30 in the morning or between 1.30 and 4.00 in the afternoon. The time of day at which the samples were taken was recorded and this was consistent throughout the study.

Plasma corticosteroid levels were measured at the beginning, at 2 weeks, and in sixteen of the thirty-four patients, at 4 weeks after commencing treatment with clobetasol. When a patient's lesions were healed after 2 weeks' treatment and no further hospital visit was necessary, the plasma corticosteroid level was not assayed again at 4 weeks. The amount of ointment issued was recorded and at the end of the 2 and 4 week treatment periods all unused tubes were recovered so that the total amount of ointment used could be assessed. No patient received any other topical steroid preparation.

Thirty-five patients (twenty-two male and thirteen female) between the ages of 23 and 67 years were studied. Fourteen of the patients had eczema, seventeen patients had psoriasis and four had lichen planus. One patient was unable to complete even a 2-week period of treatment because of domestic circumstances, the remaining thirty-four patients applied clobetasol ointment twice daily, without occlusion, for either 2 or 4 weeks.

RESULTS

After applying clobetasol ointment for at 2 weeks, one patient's lesions (patient 1) were worse. This patient then discontinued the treatment, although on a later occasion, when clobetasol treatment was recommenced, the lesions improved. Fourteen patients stopped applying the ointment after 2 weeks because their lesions cleared. Of the remaining nineteen patients, eighteen had shown an improvement after 2 weeks, and one patient with lichen planus (patient 13) had experienced no change. After 2 weeks further treatment, seven patients' lesions continued to improve, in seven they were cleared, one patient with eczema showed no further improvement (patient 15) and one patient with pustular psoriasis (patient 12) became worse.

The patients involved in this study were a typical section of those out-patients normally receiving topical steroid therapy in a dermatological clinic. Half the patients (Table 1) had 5% or more of the total body surface affected by their disease (range 5–80%). Consequently, a wide range was seen in the amount of topical steroid applied per week (4–180 g ointment per week).

The mean plasma corticosteroid level was 13.3 μg/100 ml (range 3–25 μg/100 ml) prior to treatment, compared with a mean level of 13·0 μg/100 ml (range 1–24 μg/100 ml) after 2 weeks' treatment with clobetasol ointment. The lower limit of normal adrenal function was taken as $\geqslant 6$ μg/100 ml. Thirty patients (86%) had normal plasma corticosteroid levels throughout the whole period of study. Two out of thirty-five patients had an initial plasma corticosteroid level below normal, two out of thirty-four patients and three out of sixteen patients had low plasma corticosteroid levels after 2 and 4 weeks treatment respectively (Table 1).

TABLE 1. The effect of clobetasol propionate ointment on plasma corticosteroid levels

Patient		Area involved (%)	Amount of steroid used (g/week)	Plasma corticosteroid level (μg/100 ml)		
				Initial value	After 2 weeks	After 4 weeks
1	M.B.	<5	37	13*	22*	—
2	H.C.	20	—	17*	—	—
3	A.L.	20	60, 40	8	11	25
4	S.R.	<5	40, 27	12	10	9
5	F.H.	5	43, 42	6	6	9
6	E.C.	<5	20	20*	20	—
7	A.B.	40	93, 90	12*	15*	16*
8	R.W.	<5	15, 11	10	11	9
9	P.L.	20	114	5	8	—
10	R.H.	20	116, 90	3	3	5
11	T.C.	<5	10, 10	13*	17	8
12	E.P.	<5	8, 8	9	10	5
13	A.S.	<5	25	19	27	—
14	K.B.	20	30	8	12	—
15	P.M.	<5	30, 15	12*	9*	11*
16	A.B.	40	103, 120	11	1	10
17	V.O.	<5	30	19	15	—
18	Q.V.	20	30	25	19	—
19	L.M.	5	72, 57	18*	15*	13
20	L.K.	20	30	14	11	—
21	A.G.	<5	4, 4	14*	15	16
22	M.M.	<5	4	22	13	—
23	Y.W.	80	120	12*	12	—
24	G.K.	<5	30	23	24	—
25	C.T.	80	90	11	14	—
26	J.K.	<5	23	11	13	—
27	G.F.	<5	8	14*	14*	—
28	E.C.	5	48	14*	14*	—
29	S.H.	80	150	13	13	—
30	E.P.	<5	23, 15	12*	15*	11*
31	E.C.	5	98, 75	11	9*	10*
32	R.G.	<5	43, 33	13	7	5
33	L.A.	10	180, 137	16	11	10
34	I.B.	5	37	13	10	—
35	B.J.	<5	15	14	16	—

* Blood samples taken in the morning.

DISCUSSION

The results of this study showed that thirty out of thirty-five patients had normal plasma corticosteroid levels at the beginning and end of a period of treatment with clobetasol ointment. Two patients (patients 9 and 10) had a plasma corticosteroid level below normal before beginning treatment with clobetasol. Patient 9, who had an initial level of 5 μg/100 ml, had not applied any topical steroids at all during the week prior to commencing the study. This low level may have been related to the fact that

blood sampling was carried out in the afternoon. Two weeks after applying the ointment to approximately 20% of the total body surface (114 g/week) the plasma corticosteroid level was 8 μg/100 ml. Patient 10, who had an initial plasma corticosteroid level of 3 μg/100 ml, had been applying more than 50 g/week of betamethasone valerate ointment with occlusion. This patient, who had 20% of her body surface covered with psoriatic lesions, applied 116 and 90 g/week of clobetasol without occlusion and during this time the plasma corticosteroid levels remained suppressed (3 and 5 μg/100 ml respectively after 2 and 4 weeks treatment.)

Only one patient (patient 16) who began the study with a normal initial plasma corticosteroid level (11 μg/100 ml) had a depressed level (1 μg/100 ml) after 2 weeks treatment with clobetasol. However, although this patient continued to apply the ointment at the same rate (more than 100 g/week) for a further 2 weeks, the plasma corticosteroid level returned to normal (10 μg/100 ml). One possible explanation for this finding is that the healing of the lesions during this period restored the barrier to penetration by the steroid (Scoggins & Kligman, 1965).

Patients 12 and 32, who were diagnosed as having pustular psoriasis and eczema respectively, had less than 5% of their total body surface affected by their disease. Although patient 12 was only applying 8 g/week of clobetasol ointment for 4 weeks, at the end of this time her plasma corticosteroid level had dropped to 5 μg/100 ml. This is an anomaly as this result would not have been expected because of the small amount of body surface affected and the amount of steroid used. Patient 32 applied a larger amount of ointment (43 and 33 g/week) to both feet, the only areas affected, and his plasma corticosteroid level continued to fall (Table 1) throughout the 4-week period of treatment (13, 7 and 5 μg/100 ml respectively).

Whether or not the final plasma corticosteroid levels in these two patients were a result of treatment or merely examples of lower values which might be expected when sampling in the afternoon, would only be established by a more stringent test of pituitary–adrenal function than the one we used. However, it should be noted that four patients (patients 7, 23, 25 and 29) who were using between 90 and 150 g/week with 40–80% skin involvement did not show any depression of plasma corticosteroid levels.

The limitations of random plasma corticosteroid levels as a measure of adrenal function must be appreciated; the more exacting insulin stress test is needed to determine if adrenal responsiveness is suppressed even though a normal plasma corticosteroid level is obtained.

CONCLUSION

Clobetasol propionate is a highly effective topical steroid in the treatment of eczema and psoriasis. The pattern in this study confirms the previous findings (Wilson *et al.*, 1973; Munro & Clift, 1973) that only a very small proportion of patients being treated with potent steroids topically have plasma corticosteroid levels below normal. Short courses of a highly effective treatment, which is then withdrawn until a relapse occurs and which produce only very transient adrenal suppression in a minority of patients would seem preferable to prolonged treatment with a less active steroid. Thus not only would systemic consequences be avoided but the possibility of the more troublesome local side effects would also be lessened.

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