

## SYSTEMIC EFFECTS OF LOCAL TREATMENT WITH HIGH DOSES OF POTENT CORTICOSTEROIDS IN PSORIATICS

John Eskil Nilsson and Lennart Josef Gip

*Department of Dermatology, Sundsvall Hospital, Sundsvall, Sweden*

**Abstract.** The risk of systemic effects of high doses of potent topical corticosteroids was evaluated in 6 psoriatics with lesions on more than 50% of the body surface. Before the examinations the patients had been treated for 3-4 months with 35-65 g fluorinated corticosteroids daily. General clinical examination, plasma cortisol determinations, and tetracosactrin tests were carried out. One patient showed clinical signs of Cushing's syndrome including diabetes mellitus, another had a slight Cushingoid appearance. The plasma cortisol levels were depressed in 5 of the 6 patients on the first post-treatment day. A subnormal plasmacortisol response to tetracosactrin stimulation was noted in 3 of the patients. In these cases the potent corticosteroid therapy was discontinued. One month later a follow-up was performed, which showed a clinical and laboratory normalization except for the tetracosactrin test in one case. The study emphasizes the risk of serious systemic effects of the absorbed corticosteroids, if high doses are used for long periods.

**Key words:** Topical corticosteroids; Psoriasis; Systemic effects

It is common knowledge that corticosteroids used topically in the treatment of skin diseases may be absorbed to some extent. Highly potent corticosteroid preparations involve a greater risk of systemic effects and possibly the development of an iatrogenic Cushing-syndrome. Staughton et al. (5) reported four cases of Cushing's syndrome after treatment with high doses of Clobetasol-propionate (Dermovat), which is probably one of the most potent topical corticosteroids available today. In 1977 (3) we presented a case of iatrogenic Cushing syndrome after excessive local treatment with desoxymethasone (Ibaril) and betamethasone valerate (Celestona valerat). As the most potent topical corticosteroids are now widely used for many skin diseases, the problem of their systemic effects is obviously becoming increasingly important.

The aim of this retrospective study was to evaluate the risk of systemic effects in psoriatics

who have been using high doses of potent corticosteroids for long periods.

### MATERIAL

#### *Patients*

Six adult patients (1 woman and 5 men, age range 35-58 years) with psoriasis were selected. The range of duration of psoriasis in these patients was 8-15 years. They were suffering from an exacerbation of 2-5 months' duration. Psoriatic lesions covered more than 50% of the body surface in all the patients. None had used topical or systemic steroids during the last 6 months. They were now treated with topical fluorinated corticosteroids because Ingram or PUVA regimes had failed and corticosteroids had a beneficial effect on the disease. With the exception of psoriasis, the patients were healthy. None of them revealed any symptoms or signs of liver disease.

#### *Duration of treatment*

The patients had treated themselves at home with topical corticosteroids applied twice daily for 3-4 months. None had used occlusive dressing. No other relevant medical treatment had been given during this period.

#### *Preparations*

Each patient had used 2 or 3 different preparations. The vehicles used were creams or ointments. The preparations used are listed in Table I, in either of two classes, I and II. It is generally accepted that the preparations in class II are more potent than those in class I.

#### *Quantity of preparations used*

The calculated quantities of preparations used daily by each patient are listed in Table II. The patients are divided into two groups, A and B, as shown in the table. The

Table I. *Classes of potency of used preparations*

- |     |  |
|-----|--|
| I.  | Flumetasone pivalas, acid. salicyl. 3% (Locasalen)<br>Betamethasone valerate (Celestona valerat)       |
| II. | Betamethasone dipropionate (Diproderm)<br>Desoxymetasone (Ibaril)<br>Clobetasol. propionate (Dermovat) |

Table II. Amount of topical steroid used

Patient		Preparation g/day	
Group	No.	Class I	Class II
A	1	40	
	2	40	
	3	50	
B	4	20	15
	5	10	25
	6	20	45

patients in group A had used preparations exclusively from class I. The patients in group B had used preparations both from class I and class II.

## METHODS

### Clinical examination

The patients were all hospitalized. A general clinical examination was performed with special reference to signs of Cushing's syndrome.

### Routine laboratory investigations

Blood examinations, including white blood cell count, red blood cell count, haemoglobin, haematocrit, serum alanine-aminotransferase, creatinine and electrolytes were performed. Routine urine analysis for sugar, protein, and red and white cells was performed.

### Tests for adrenal suppression

Administration of corticosteroids inhibits ACTH secretion by the pituitary and this in turn results in cessation of synthesis and secretion of corticosteroids by the adrenal. This is an invariable response to corticosteroid administration in all subjects with a normal hypothalamo-pituitary-adrenal axis. When the corticosteroid dose is high, or administration frequent, the periods of acute inhibition may follow each other too closely to permit recovery between doses. As a result the adrenal cortex may be more or less permanently deprived of stimulation by ACTH. Deprivation of ACTH causes gradual loss of adrenal sensitivity and if the deprivation is prolonged, atrophy of the cortex ensues. Concerning these physiological facts it is obvious that a standardized plasma cortisol determination and a short tetracosactrin test (6) are two of the most pertinent investigations for studying the systemic effects of synthetic corticosteroids. These tests were therefore chosen for this study; they were performed in the following way.

The topical corticosteroid was discontinued. The following day, blood was sampled for plasma cortisol at 8 a.m. A few minutes later 0.25 mg of tetracosactrin (Synacthen) was injected intramuscularly and blood was sampled half an hour later for plasma cortisol. Plasma cortisol estimations were carried out in the same laboratory using a radio-immuno-absorbent method.

The normal plasma cortisol range for the resting subject at 8 a.m. is 330-1000 nmol/l. A normal response to an

injection of 0.25 mg of tetracosactrin is recorded if after 30 min plasma cortisol levels have risen by at least 220 nmol/l.

## RESULTS

### Clinical examination

Clinical examination of the patients revealed that patient no. 5 had a suspected Cushingoid appearance with a slight moon face and buffalo hump. Patient 6 complained of thirst and had a moon face, buffalo hump, central obesity and striae, i.e. he had an obvious Cushing syndrome (Fig. 1). The other patients were normal on physical examination except for the presence of psoriatic lesions.

### Routine laboratory investigations

In patient 6 the white cell count was 8 900/mm<sup>3</sup>. The differential white cell count showed a relative

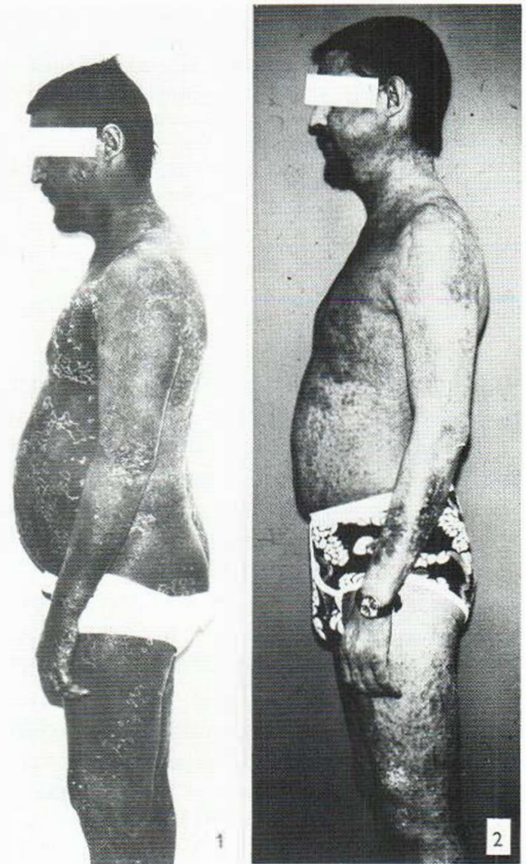


Fig. 1. Post-treatment Cushingoid habitus of patient 6. Fig. 2. Normalized status of patient 6 one month after cessation of treatment with potent corticosteroids.

Plasma cortisol 8 a.m.  
(normal range 330-1000 nmol/l).

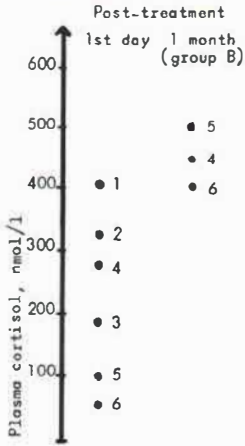


Fig. 3

lymphopenia with 6% (normal 25-45%) lymphocytes. The fasting blood glucose value was 6.54 mmol/l (normal 2.78-5.55 mmol/l) and the glucosuria 43.6 mmol/24 h. The routine laboratory investigations in the other 5 patients were within normal limits.

#### Plasma cortisol

The plasma cortisol levels on the first post-treatment day were depressed in 5 of the 6 patients. Patients 5 and 6 from group B showed the lowest levels (Fig. 3).

#### Tetracosactrin test

The patients in group A showed a normal response to tetracosactrin. The patients in group B demonstrated a subnormal plasma cortisol response to the tetracosactrin stimulation. Patient 6 had the lowest response (Fig. 4).

#### One month follow-up of group B

Administration of potent topical corticosteroid preparations was discontinued in the group B patients, who were put on a hydrocortisone acetate preparation (Ficortril), 30-40 g daily. This could be done without any signs of acute adrenal insufficiency developing in the patients. One month later a follow-up investigation was undertaken. Clinical examination, routine laboratory investigations and tests for adrenal suppression were performed and the following results were noted. A normalization

of the physical status in the patient with Cushing's syndrome had taken place (Fig. 2). Routine laboratory investigations and the plasma cortisol levels were normal (Fig. 3). Tetracosactrin tests were normal in patients 4 and 5. The response to tetracosactrin injection was increased in patient 6, but was still sub-normal (Fig. 4).

#### COMMENT

Schlagel & Sanborn (4) have shown that 30 g of an emollient was at the upper range of the quantity required to give a sparing application all over the body of an average adult. The psoriatics investigated in this study had used from 35 to 65 g ointment per day. These doses are very high, but according to Schlagel & Sanborn the figures are realistic if one wants to treat psoriatic lesions covering more than 50% of the body surface, twice daily.

Unfortunately, there is no simple correlation between the value of the tetracosactrin test and the dose of absorbed corticosteroid. We would like to recall two investigations made in patients who had been treated with peroral corticosteroids for long periods. In one study (1), on 39 rheumatoid arthritis who had received 5 mg or less of prednisone daily for periods varying from 8 weeks to 8 years, only 4 showed an abnormal tetracosactrin test. In another study (2), on 19 rheumatoid arthritis who had received 5-15 mg daily from 9 months to 8 years, 6 out of 19 patients revealed an abnormal 30

Increase in plasma cortisol  
30 min after 0.25 mg Tetro-  
cosactrin given i.m. 8 a.m.  
(normal response  $\geq 220$  nmol/l).

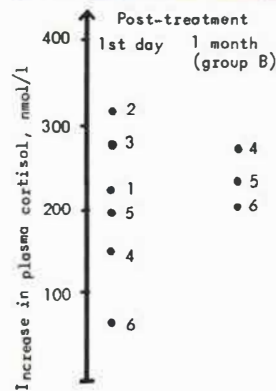


Fig. 4

min tetracosactrin test. In general the abnormal response tended to arise in those who had received the largest total dose of corticosteroids. In our study 3 out of 6 patients showed a subnormal response to tetracosactrin injection. These 3 patients had been treated with the most potent corticosteroids.

Our study has shown that, in psoriatics, there is a clinical risk of systemic effects from the absorbed corticosteroid only when high doses of the most potent preparations are used for long periods over wide areas of the body. In cases of psoriasis where the most potent topical corticosteroids are used, then it is important that a keen watch is kept on the doses of corticosteroid preparations used and on the duration of treatment. It is even necessary to be aware of the risk of acute adrenal insufficiency if the treatment is stopped suddenly. A gradual withdrawal is to be recommended in order to avoid withdrawal symptoms and rebound phenomenon of the disease. If there is a suspicion of a serious adrenal suppression, a tetracosactrin test ought to be performed before further treatment schedules are planned. The present study has shown that even when the patient has got quite a serious systemic effect from the absorbed corticosteroid, one could expect a normalization of the adrenal responsive-

ness as soon as one month after treatment has elapsed.

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J. E. Nilsson, M.D.  
Department of Dermatology  
Sundsvall Hospital  
S-851 86 Sundsvall  
Sweden