Assessment of Atrophy of Human Skin Caused by Corticosteroids Using Chamber Occlusion and Suction Blister Techniques

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The effect of five corticosteroid ointments on epidermal thickness was studied using occlusive chamber application. Thinning of the epidermis and telangiectasia were noted 3 weeks after application of betamethasone-17-valerate (BV), budesonide (BD), clobetasol-17-propionate (CP), and fluocinolone acetonide (FA), but not of hydrocortisone (HC). Suction blisters were raised at the treated sites. Epidermal thinning was always associated with reduction in cell number. By combining different methods it seems possible to define more precisely the epidermal effects of various corticosteroid preparation. *Key words: Corticosteroid atrophy; Suction blister; Chamber occlusion; Microscopy.* (Received March 23, 1983.)

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Reduced epidermal thickness is a common result of prolonged topical application of potent corticosteroids. Histometric, histological, radiographic, biochemical, and other procedures are often used separately to evaluate this phenomenon. The various methods have been reviewed by Dykes & Marks (1). Experimental comparisons of different topical steroids have rarely revealed permanent changes. If chronic dermatoses are treated for long periods with potent topical steroids, permanent telangiectasia and striae may develop. However, in the treatment of psoriasis the antimitotic property of steroids is useful and essential. The signs evaluated in this study were: increase in transparency of the epidermis, flattening of dermatoglyphics, and reduction in epidermal thickness and cell numbers.

The aim of the study was to compare the epidermal thinning properties of five corticosteriod ointments applied under occlusion, using vital microscopy, histology, and histometry.

MATERIAL AND METHODS

The study was carried out on 10 volunteers, 5 men and 5 women, who had no active skin disease and who had received no corticosteroid treatment for at least 3 months before the study. Their ages ranged from 23 to 46 years (mean 35 years). Five corticosteroid ointments were tested:

betamethasone-17-valerate	BV	0.1 %	(Betnovate®, Glaxo)
budesonide	BD	0.025 %	(Preferid®, Draco)
clobetasol-17-propionate	CP	0.05 %	(Dermovate®, Glaxo)
fluocinolone acetonide	FA	0.025 %	(Synalar®, Syntex)
hydrocortisone	HC	1.0 %	(Hydrocortisone®, the National pharmacy association)

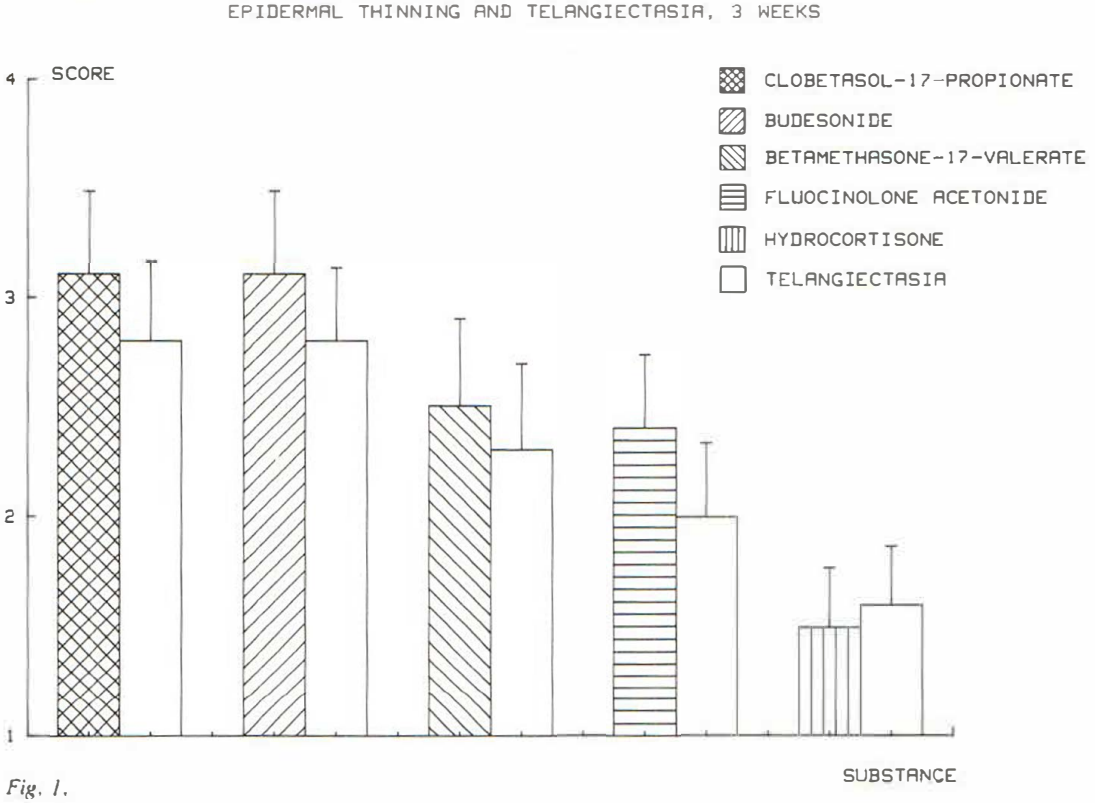

Fig. 1.

A modification of the chamber method was used for occlusion (9). About 20 µl of each ointment was placed in a Finnchamber® (Epitest Ltd. OY) which was fixed to the abdominal skin with porous adhesive tape (Scanpor, Norgesplaster A/S) for 21–23 days. The ointment was changed three times weekly and reapplied at exactly the same site. An empty chamber served as a control. Both application of ointment and evaluation of the effects were performed double-blind. Stereomicroscopy of the test sites was done on days 4, 11, and 21–23 (Wild Heerburg microscope, magnification 6–50 x). The thickness, transparency, and dermatoglyphic pattern of the skin and also the underlying vasculature were examined. The chambers were removed and the test sites cleaned with 70% alcohol immediately before microscopy. Visualization of the vasculature was enhanced by the application to the test site of mineral oil and a glass slide. Epidermal thinning and telangiectasia were evaluated by a modification of the method described by Frosch, Wendt & Kligman (2) thus:

Epidermal thinning

1. No change as compared with control test sites. (Slight flattening of dermatoglyphics due to hydration was regularly found at control sites.)
2. Slight increase in transparency and slight flattening of dermatoglyphic pattern.
3. Moderate thinning of epidermis with moderate increase in transparency; flattened dermatoglyphics.
4. Severe thinning and increased transparency, markedly flattened dermatoglyphics.
5. Very severe thinning of epidermis with complete loss of dermatoglyphics; vasculature clearly visible.

Telangiectasia

1. Normal vascular pattern
2. Capillary hyperaemia with slight elongation and dilatation of some vessels, not visible to the naked eye.
3. Moderate telangiectasia, barely visible to the naked eye.

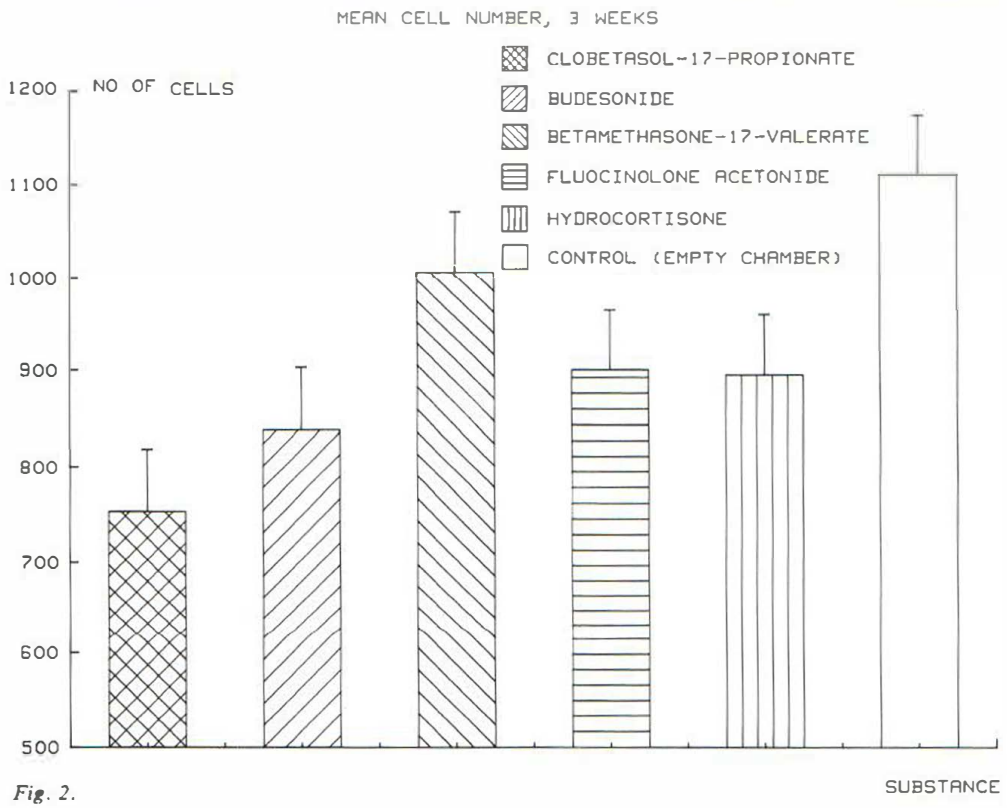

Fig. 2.

4. Severe telangiectasia with marked reduction of capillary loops.
5. Very severe telangiectasia, with complete absence of capillary loops.

After microscopy on days 21–23, suction blisters were raised at the test sites (4). During suction, the pressure varied between −180 and −210 mmHg and the temperature between 37 and 45°C. The suction time was recorded. From 4 subjects the tops of the blisters were removed, and an attempt was made to weigh them. However, since the size of the epidermal areas varied, the results were not reliable. The remaining blister tops were therefore prepared for routine histological examination using haematoxylin–eosin staining. Cell counts of each epidermis sample were made over 3 mm, the distance being measured along the outer margin of the epidermis. The area and mean thickness of the 3-mm-long epidermal section were measured. Using a projector microscope the image of the epidermis was projected onto a screen and drawn on graph paper, marked in millimeters, and the distance and area were measured from these drawings. Statistical analysis was performed using the Friedman test or two-sided analysis of variance for each variable assessed.

RESULTS

Microscopic evaluation of atrophy and telangiectasia

4 days: No epidermal thinning or telangiectasia. 11 days: Moderate thinning and telangiectasia. 21–23 days (Fig. 1): CP and BD caused significant epidermal thinning and telangiectasia ($p<0.01$ Friedman test). BV and FA caused less pronounced changes. HC was the least atrophogenic.

Suction time and healing

The total suction time varied from 1 h 20 min to 2 h (mean 1 h 40 min). The time from commencing suction to the first sign of blister formation ranged from 18 to 63 minutes

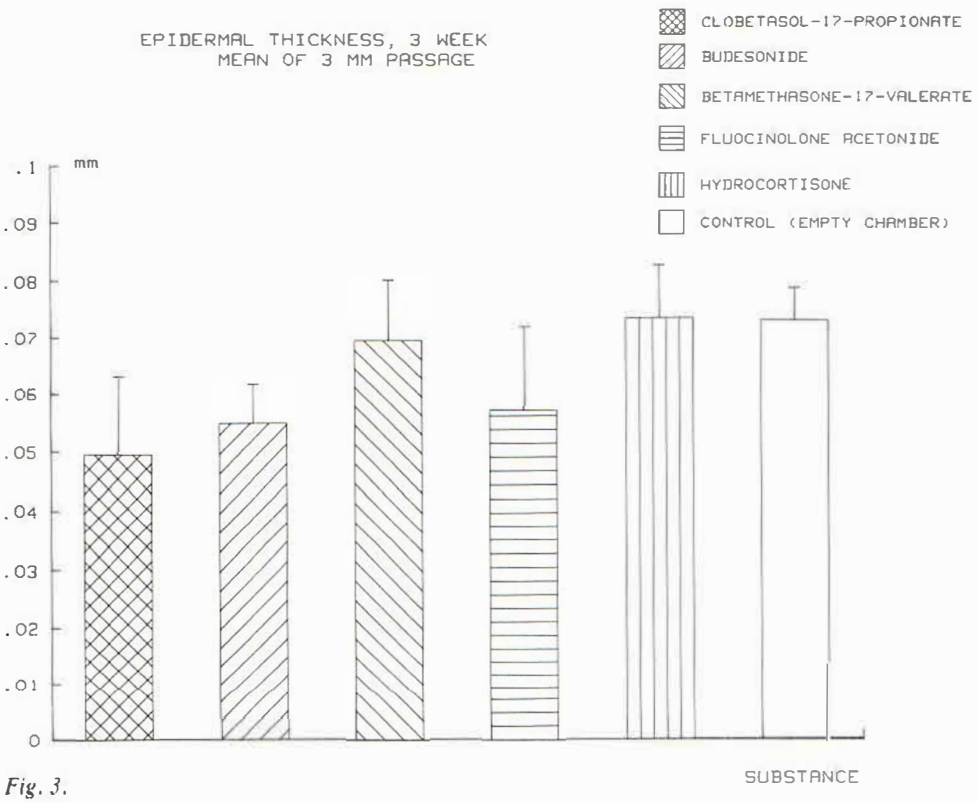

Fig. 3.

(mean 41 min). The formation of blisters was hastened by increasing the temperature and the suction pressure. Suction time was apparently not affected by the steroid treatment.

Epidermalization of the blister base took from 5 to 10 days. No scarring occurred. Pigmentation of the test sites developed in most subjects. Depigmentation also took place. This faded gradually, but in a few subjects did not disappear completely during the 6-month observation.

Cell counts and epidermal thickness

The greatest reductions in epidermal cell count were caused by CP and BD (Fig. 2) ($p<0.05$, two-sided analysis of variance). BV did not affect cell numbers, and HC and FA caused a moderate reduction.

The thickness of the epidermis was also clearly reduced. This effect was most prominent at sites treated with BD, CP, and FA (Fig. 3). Comparison with the controls showed that the difference was significant ($p<0.01$, two-sided analysis of variance).

DISCUSSION

In this investigation, application of corticosteroids was apparently invariably associated with telangiectasia. Striae and telangiectasia caused by steroids probably indicate damage to dermal collagen. The explanation why steroids produce telangiectasia may be atrophy of the supporting collagen around the vessels.

The non-halogenated BD caused more pronounced epidermal thinning than did BV and

FA, but the difference was not significant. This is consistent with findings concerning its vasoconstrictor potency (3). BD seems to be less potent systemically than topically (8). Other studies have shown that halogenation is not necessary for potency or epidermal thinning properties (2). The descending order of potency for production of atrophy by steroids seems to be CP, BD, BV, FA, and HC. However, the effects of FA and BV were very similar.

In the past, evaluation of epidermal and dermal changes induced by topical corticosteroids has been controversial. The antimitotic properties of steroids are necessary in the treatment of psoriasis and other hyperproliferative skin diseases. Although atrophy has been regarded as being one of the most serious adverse effects of topical steroids, its significance is unclear. Permanent changes are rarely encountered, but slight reversible atrophy is relatively common.

Counting of epidermal cells was needed because hydration could have enlarged the cells and hence increased the epidermal thickness. The technical problems in the determination of epidermal thickness are well recognized (6). The blister tops were relatively easy to spread out and did not shrink as much as whole-skin samples, facilitating histological processing. Because each method has disadvantages when used alone, it seems reasonable to combine different procedures. If the results of both procedures show the same tendency, as in this study, the effects of the disadvantages of each can be reduced.

The chamber method proved to be a practical means of prolonging topical steroid testing. When chambers are attached to the abdominal skin they caused minor skin damage, which does not occur on arms, thighs, or dorsum. The suction blister equipment used in this study is best suited for suction of abdominal skin. The area of the chamber is adequate for both microscopy and suction blisters.

Epidermal thinning is usually evaluated by biopsy, but large areas of skin cannot be excised. Instead a suction blister can be raised. The technique leaves no scar, but the dermal changes cannot be examined histologically. However, the blister fluid can be analysed, and the blister base can be examined by stereo-microscopy.

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