

EFFECTS OF FLUOCINOLONE ACETONIDE CREAM ON THE SKIN WINDOW RECORD OF INFLAMMATORY EXUDATES*

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ABSTRACT

In order to study the pathophysiologic mechanism of steroidal action at a cellular level, the skin window technique was used in determining the effect of topically applied fluocinolone acetonide cream under plastic occlusion.

Fluocinolone acetonide cream was applied to the normal skin of the volar aspect of each subject's forearm. The cream was left on for twenty four hours in six subjects and ninety six hours in another six subjects. Skin window abrasions (inflammatory stimuli) were then performed on the area where the cream had been applied. A control abrasion was done on the untreated forearm.

No change in differential counts done on coverslips from control versus fluocinolone acetonide cream treated areas could be found using ranking of paired comparisons as a means of analysis.

This investigation suggests that this topically applied steroid does not exert its anti-inflammatory effect by suppressing polymorphonuclear cells, mononuclear cells, eosinophiles or basophiles.

Besides clinical observations on the effectiveness of topical steroids, several laboratory models have been developed to quantitate this effectiveness, such as, inhibition of ultraviolet erythema (2, 3, 4) suppression of chemical irritation (5, 6), and degree of vasoconstriction (7-9). Delving further, Weissman (10) has studied the effects of steroids at a biochemical level (lysosomal stabilization). This skin window study was undertaken to examine a topical steroid's effect at the cellular level.

MATERIALS AND METHOD

Subjects were selected from the general dermatology wards. Two subjects had hypertrichosis, 2, primary irritant dermatitis of the hands, 2, venous stasis ulcers, 2, seborrheic dermatitis, 1, rosacea, 2, psoriasis, and 1, lichen simplex chronicus. Seven of the subjects were females and five males. Their ages ranged from 14-71 years.

This study was carried out with the support and advice of Professor G. Asboe-Hansen, Department of Dermatology, University of Copenhagen, Rigshospital.

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Received July 6, 1971; accepted for publication July 14, 1971.

Two tenths of a milligram of 0.2% fluocinolone acetonide cream¹ was applied to a 3 × 3 cm area of normal skin on the volar aspect of the right forearm. This area was then occluded with a square of plastic² for 24 hr in 6 subjects and 96 hr in the other 6 subjects.

After the time periods had elapsed, a fine film of Synalar® cream remained on the skin and it was removed with an alcohol sponge. A 1 cm² area of skin was abraded (inflammatory stimulus) with a scalpel until fine bleeding points were seen on both the left (control) and right (fluocinolone acetonide treated) forearms. A drop of saline was applied to both abraded areas and covered with a sterile, cardboard-backed coverslip. Following the initial abrasion, the coverslips were changed at 3, 6, 9, 12, 18, 21, 24, 27, 30, 33, 42, 45, 48, and 51 hours. The coverslips, which dry quickly, were then all stained at one time by the method of May-Grünwald-Giemsa.

Differential counts were done on each coverslip. Between 200 and 500 cells were counted by passing a pointer systematically over the entire coverslip, recording all those cells which fell under the pointer.

RESULTS

All the coverslips were assessed as to percentages of the various cell types they carried: polymorphonuclear cells, mononuclear cells, eosinophiles and basophiles. The percentages of the cell types from the paired coverslips (control

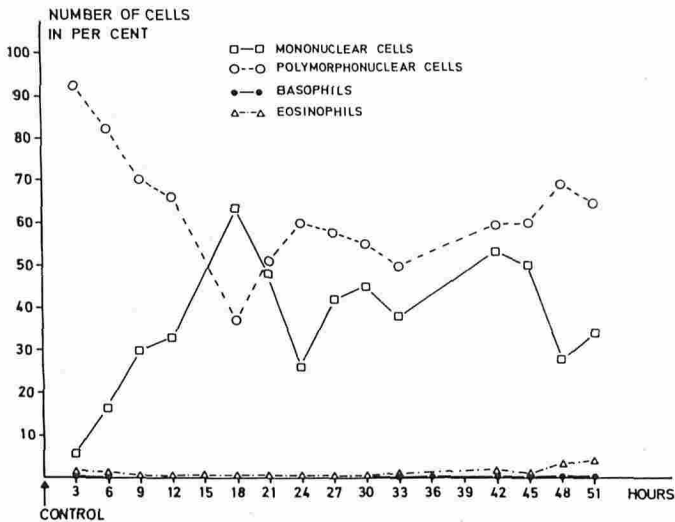
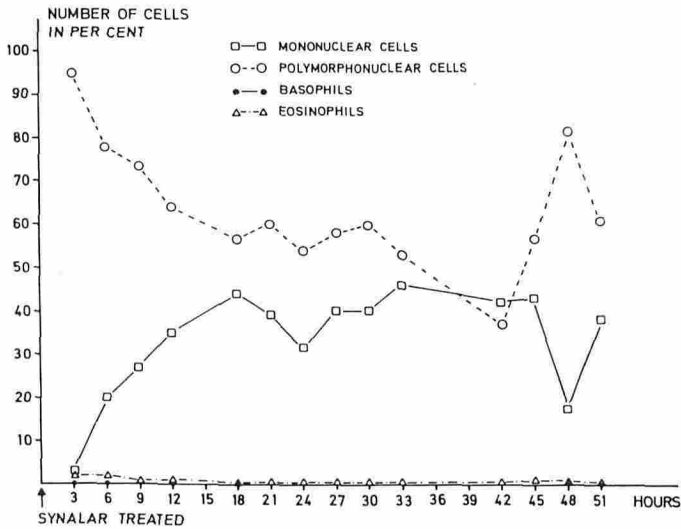
¹ Synalar® (Syntex)

² Parafilm® (American Can Co.)

and fluocinolone acetonide treated) at 24 and 96 hours were compared in two ways. Averages of the percentages of the cell types at each hour (combined 24 and 96 hr coverslips) were graphed. See Figures 1 and 2.

A rank test (11) was also applied to the paired comparisons, control and Synalar® treated, at each hour (combined 24 and 96 hr coverslips). No significant difference was found in the ranking at any hour except the eighteenth. At that hour, the polymorphonuclear cell percentage was

less in the control ($P = 3\%$), and the mononuclear cell percentage was higher in the control ($P = 1\%$). Two subjects at this time had contamination of their coverslips with bacteria. Excluding them from the eighteenth hour rank comparisons, the greater mononuclear cell percentage in the control remained significant ($P = 5\%$), while the polymorphonuclear cell depression did not. Excluding bacterially contaminated coverslips from the other hours' rank comparisons did not change the significance levels.



Averages of the percentages of the cell types found on the skin window coverslips of twelve subjects are shown. The hours given indicate the times at which the coverslips were changed following the initial skin window abrasion at zero hour.

The subjects who had their occlusive dressings on for ninety six hours were separated from the twenty four hour ones and analyzed by ranking. No significant difference ($P < 5\%$) occurred between the paired comparisons, control and fluocinolone treated, over the fifty one hour period of study.

Fortuitously some subjects developed skin window eosinophilia and basophilia at various hours. Twenty paired comparisons of eosinophile percentages (as high as 5.5%, 8.8% and 16% in fluocinolone treated areas) were ranked. No significant difference between the control and fluocinolone treated areas occurred at $P < 5\%$. Nine paired comparisons of basophile percentages were analyzed by ranking, and no significant difference was found. None of the subjects had basophilia or eosinophilia on their peripheral blood smears.

DISCUSSION

The fluocinolone acetonide treated areas had a white appearance (delayed blanch) prior to abrasion. This observation plus studies on the effect of plastic occlusion on the absorption of radioactive labelled topical steroids (4, 12) suggest that there was absorption of the fluocinolone acetonide cream used in this study.

After this assumed absorption of fluocinolone acetonide, the inflammatory stimulus (skin window abrasion) was applied. No suppression of one cell type versus another could be found except at one hour where the significance levels were not great.

Although it is well known that systemically administered steroids suppress the total number of cells found on skin window coverslips (13, 14), studies of the differential cell counts found on skin window coverslips differ with respect to systemic and topically administered steroids. Rebuck *et al.* (13) found a depression of the percentages of eosinophiles and mononuclear cells after systemic steroids whereas Boggs (14) found no such suppression. Edinger *et al.* (15), in agreement with Rebuck, found a depression of skin window eosinophilia by systemic steroids.

Edinger *et al.* (15) did not find a depression of skin window eosinophile percentages after topical steroids. Weiss (16) doing skin windows and Juhlin (17) cantharidin blisters did find a suppression of the percentages of eosinophiles

after topical steroids. Juhlin (17) used fluocinolone acetonide under occlusion prior to applying the cantharidin; thus the same steroid and the same method of application were used in his and this study. However in this investigation no suppression of skin window eosinophilia by fluocinolone acetonide cream was found.

Rebuck and Mellinger (18) found that topically applied cortisone, to abraded skin window areas, inhibited the ability of neutrophils to phagocytize India ink particles. In this investigation, a few coverslips had bacterial contamination. But in contrast to Rebuck and Mellinger's findings, bacteria were seen to be in the cytoplasm of many polymorphonuclear cells, presumably phagocytized. Both control and fluocinolone treated areas had phagocytized bacteria.

In conclusion, this investigation did not show any effect of occluded topical fluocinolone acetonide on the cellular inflammation revealed by the skin window technique.

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