BETAMETHASONE INDUCED HISTOLOGICAL CHANGES IN THE GUINEA PIG SKIN

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Corticosteroid induced histological changes were studied in the skin of the guinea pig. Betamethasone-17-valerate (0.1%) ointment was applied twice daily to a small area of animal's dorsal skin. Skin samples were excised from the treated areas every week for four weeks. Histological study was carried out under light microscope. The study revealed mild atrophic changes in the skin after the 4th week.

INTRODUCTION

Corticosteroid induced cutaneous atrophy is a well recognised feature of prolonged topical use of potent corticosteroids. Although the original phenomenon was described by Epstein *et al.* (1963) yet the experimental evidence in this area was not forthcoming until recently. To establish a minimum time scale for inducing skin atrophy with a potent topical corticosteroid that would accomplish its safe usage, the experiment under report was carried out.

MATERIALS AND METHODS

Male Albino guinea pigs weighing 500 ± 25 g were shaved on the back with electric clippers. They were stabilized in individual cages. All animals received green fodder crushed grams and water *ad libitum*. The animals were divided into two groups A and B. The group A animals were applied betamethasone-17-valerate (0.1%) ointment, while group B acted as a control and received the base or the vehicle of the ointment. For a period of 4 weeks 0.2 ml of the ointment and the base was applied to 5 cm^2 area on the back of the animals with a glass rod, twice daily at 8.00 a.m. and then at 7.30 p.m. Four animals from each group were killed at the end of every week. Full thickness skin from the test area was excised, processed and embedded in paraffin, sectioned at 06 u vertically and studied with H and E, Van Gieson and Gomori's rapid one step trichrome stain.

For overall histological evaluation, the point scale was used (Jablonska *et al.*, 1979).

RESULTS

Table 1 indicates mild epidermal atrophy after 4 weeks topical application of betamethasone-17-valerate (0.1%) ointment. The dermal histology does not show any appreciable changes. The characteristic feature of thinned epidermis was the flattening or even complete disappearance of rete ridges. In some cases, the epidermis was composed of not more than a few layers. The reduction in number was accompanied by a decrease in size of the cells. In some sections basal cells were cuboidal in shape. Epidermal changes were often associated with signs of disordered keratinization and nuclear remnants were present in the stratum corneum. Thinning of reticular layer of dermis was observed in some sections. The collagen bundles were also thin and lightly stained. Hair follicles and sebaceous glands did not show any effect.

Epidermis	
Normal	0
Focal thinning of epidermis	1
Thinning of epidermis and flattening of rete ridges	2
Marked thinning of epidermis and flattening of rete ridges	3
Dermis	
Normal	0
Slight thinning of reticular layer	1
Distinct thinning of reticular layer	2
Distinct thinning of reticular layer and moderate degeneration of collagen with no reduction in number of fibroblasts	3
Distinct thinning of reticular layer, degeneration of collagen and marked reduction in number of fibroblasts	4
Marked thinning of reticular layer, degeneration of collagen and marked reduction in number of fibroblasts	5

The atrophogenic effect was graded as:

Nil	0
Mild	(1-2 points)
Moderate	(2-3 points)
Marked	(>4 points)

DISCUSSION

Atrophy of the skin results from long term topical application of corticosteroids especially when fluorinated (potent) steroids are used. This four weeks study was designed to evaluate the time involved to induce skin atrophy by topical application of Betamethasone-17-valerate (0.1%) ointment.

Guinea pig's skin was used for this experiment, as it formed a reasonable rodent model for human skin absorption (Andersen *et al.*, 1980). It is easy to handle and large quantities of skin can be used for testing. Ethical considerations preclude the use of human skin for such an experiment. Also the use of local anaesthetics for biopsy may cause arterfactual alterations in the skin thickness (Thomas and Black, 1985).

During first three weeks of the study, no changes could be noticed in the experimental skin. It was reported that long term application of the steroids caused skin thinning (Jablonska *et al.*, 1979). Mere application for three weeks, therefore, was not enough to induce skin thinning.

Four weeks topical application of Betamethasone-17-valerate (0.1%) showed mild epidermal atrophy. Jones (1976) observed marked epidermal atrophy within one month of topical application of Betamethasone-17-valerate (0.1%) ointment to normal human forearm skin with polythene occlusion. The dermis, however, showed slight or no changes. In this experiment, atrophy after one month's topical application of betamethasone-17-valerate (0.1%) ointment was mild rather than moderate or marked. This is so because no polythene occlusion was done. The polythene occlusion increases the rate of absorption of topical steroid and hence the effect on the skin.

The possible processes causing skin atrophy are the antimitotic and antisnythetic

Table 1. Histological evaluation of skin atrophy based on 8 points scale

Duration (weeks)	Control skin (B)			Experimental skin (A)		
	Epi.	Der.	Total	Epi.	Der.	Total
I	0	0	0	0	0	0
II	0	0	0	0	0	0
III	0	0	0	0	0	0
IV	0	0	0	1.18	0	1.18

Atrophogenic effect: Nil - 0, Mild (1-2), Moderate (2-3), Marked (>4)

effect on various components of epidermis and dermis. The epidermopoesis and collagen synthesis and fibroblast proliferation are inhibited by topical steroids (Marks, 1976). It is likely that epidermal atrophy is the first step in a sequence of changes that result in dermal atrophy and that the thinned epidermis subsequently allows a far greater penetration of steroids into the dermis to cause atrophy. The results of present study show that topical application of betamethasone-17-valerate (0.1%) ointment for four weeks causes mild atrophic changes confined mainly to epidermis.

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