The Academy of Pharmaceutical Sciences of the Pharmaceutical Society of South Africa

Comparative blanching activities of some topical corticosteroid containing lotions

by

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Abstract

The blanching activities of Betnovate and Celestoderm-V lotions (betamethasone-17-valerate, 0,1%) and Diprosone lotion (betamethasone dipropionate, 0,55%) were determined by measuring their ability to cause blanching of human skin after topical application.

Betnovate and Celestoderm-V lotions produced almost identical blanching profiles. Diprosone lotion displayed a statistically significant superior blanching acitivity over both Betnovate and Celestoderm-V lotions over the whole timespan of the trial.

Introduction

IT has been well documented that the blanching assay first described by McKenzie and Stoughton may be used as a reliable indicator of the rate of release of a cortiocosteroid from topically applied formulations (1). There is also a direct relationship between the blanching activity of a topically applied corticosteroid and its clinical efficacy (2).

This trial was performed to compare the blanching activities of two lotions containing betamethasone-17-valerate (0,1%) and one lotion containing betamethasone-17,21-dipropionate (0,05%).

Occlusion of the sites of application greatly enhances the blanching effect due to increased penetration of the corticosteroid into the skin (2), but the trial was performed in both the occluded and unoccluded mode because in practice the unoccluded mode is used most often, especially in the case of lotions which are mainly applied to the scalp and other hairy areas of the body.

The structure of the side chains at the 17 and 21 positions is probably responsible for the difference in activity of the two corticosteroids. McKenzie and Atkinson (3) reported differences in the potencies of the 17-propionate and 17-valerate esters relative to fluocinolone acetonide. Betamethasone-17-propionate was 190% more effective than fluocinolone acetonide and betamethasone-17-valerate was 360% more effective than fluocinolone acetonide when evaluated by the vasoconstriction assay. It can therefore be concluded that the 17-valerate is almost twice as potent as the 17-propionate.

It has been shown (4) that the effect of betamethasone-17,21-dipropionate is superior to that of betamethasone-17-valerate, with respect to both the blanching and therapeutic action. This illustrates the importance of the 21-propionate in the 17,21-dipropionate with respect to the structure activity relationship of betamethasone esters (Figure 1).

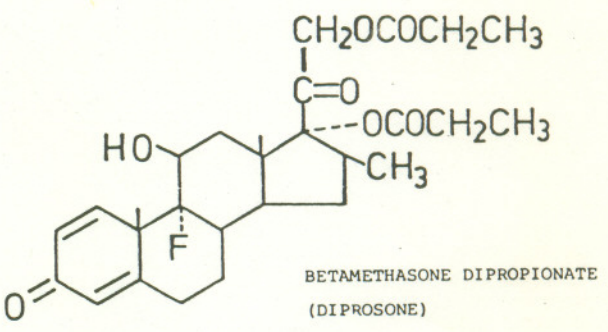
The present study therefore served the purpose of comparing the blanching activities of the two betamethasone-17-valerate containing lotions (Betnovate and Celestoderm-V) to each other and to the betamethasone-17,21-dipropionate containing lotion (Diprosone).

Materials and methods

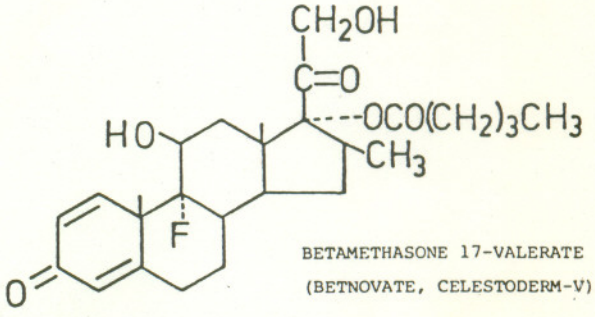
The three lotions were purchased shortly before the trial at a local pharmacy.

Twelve healthy Caucasian volunteers were selected from a panel known to show a response to topically applied corticosteroids. No reference was made to sex or steroid sensitivity. The volunteers had not received topical or systemic corticosteroids for at least six weeks prior to the investigation.

The lotions were applied to the flexor aspect of the forearm in four different arrangements, each application pattern being chosen randomly to avoid any bias during application and observation. Five microliters of the lotion (equivalent to approximately 4mg) was applied to twelve 7mm square sites on each forearm of the volunteers in a double blind fashion using a micro-pipette. The pipette was also used to spread the lotions immediately after application. ▶



BETAMETHASONE DIPROPIONATE
(DIPROSONE)



BETAMETHASONE 17-VALERATE
(BETNOVATE, CELESTODERM-V)

Figure 1

In the occluded mode the sites were covered with a non-porous plastic covering (Blenderm Surgical tape) and the non-occluded sites were protected by cardboard coverings cut in such a way so as to allow a free flow of air.

The residual steroid was removed from all the sites six hours after application by gentle washing with soap and warm water. The degree of blanching for each site was recorded independently by three experienced observers at 7, 8, 9, 10, 12, 14, 16, 18 and 28 hours after application using a 0-4 scale:

0 = normal skin
1 = slight vasoconstriction
2 = more intense vasoconstriction
3 = general even vasoconstriction with distinct blanching
4 = marked vasoconstriction with very distinct blanching

The methods used to evaluate the results were the area under the curve (AUC), the number of sites exhibiting blanching, the graded intensity of vasoconstriction and a paired comparison of adjacent sites (5). Blanching profiles (Figures 2 and 3) were obtained using the percentage of the total possible score and the time in hours after application.

Results and discussion

In the occluded mode the AUC for Diprosone was greater than that of Celestoderm-V which was greater than that of Betnovate. In all the methods of analysis there was no significant difference between Betnovate and Celestoderm-V (except the graded response at 16 hours which was in favour of Celestoderm-V), and Diprosone was significantly better in all the methods of analysis at most of the time intervals — especially at the peak times, i.e. between 8 and 18 hours after application.

The AUC in the unoccluded mode was greatest for Diprosone with Betnovate and Celestoderm-V giving very similar values. All the other methods of analysis gave results of Diprosone being significantly better than Betnovate and Celestoderm-V. No significant differences were exhibited between Betnovate and Celestoderm-V.

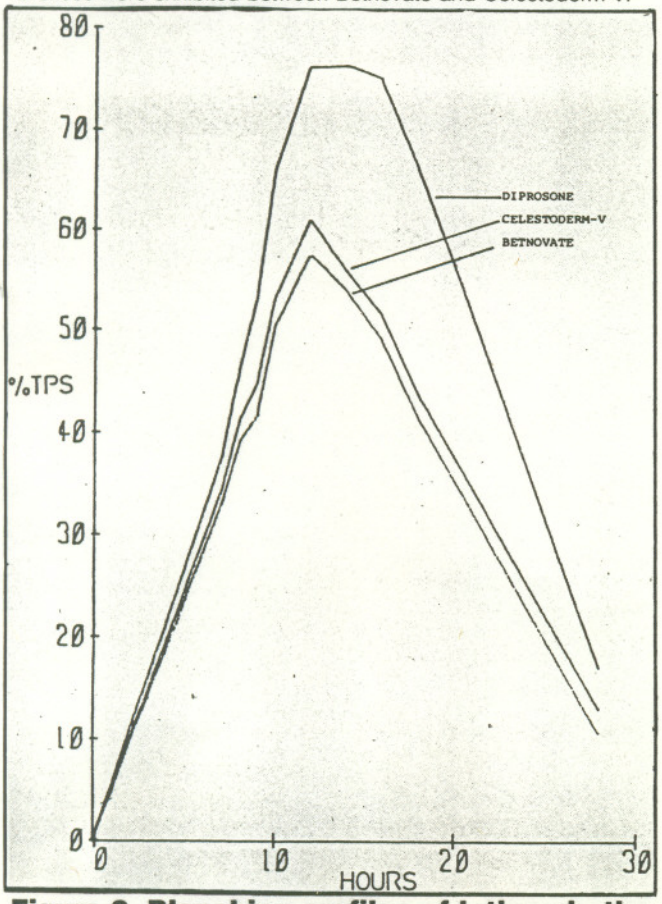


Figure 2. Blanching profiles of lotions in the occluded mode.

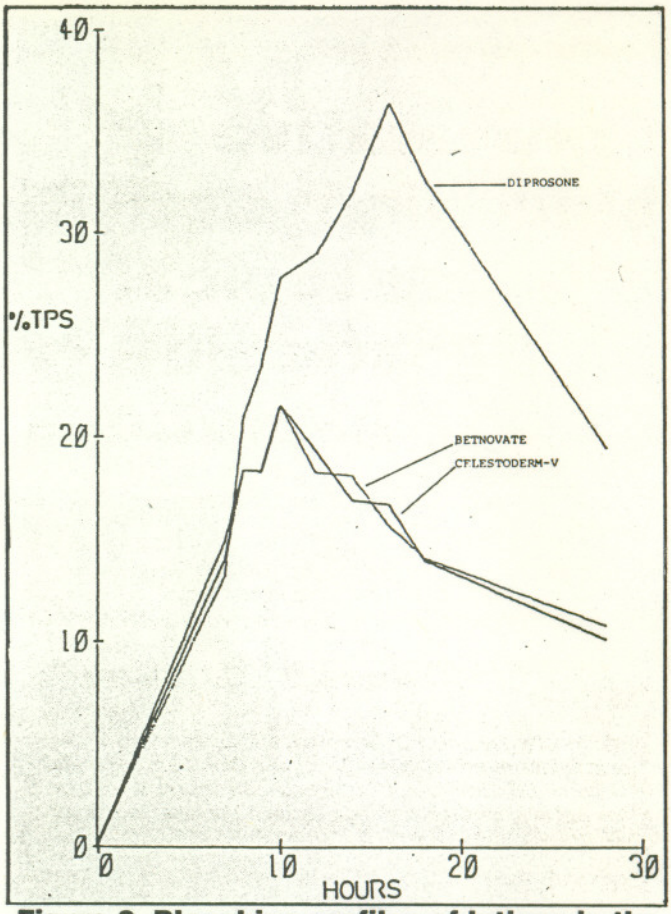


Figure 3. Blanching profiles of lotions in the unoccluded mode.

The main conclusions that can be drawn from this trial are that:

(i) Diprosone lotion has a statistically significant superior blanching activity over Betnovate lotion and Celestoderm-V lotion, even though the concentration of the corticosteroid in Diprosone lotion is half of that of the other two lotions. It would be expected that if these lotions were formulated containing the same concentration of corticosteroid, the differences in the blanching activities would be even more marked.

(ii) There are no statistically significant differences between the blanching activities of Betnovate lotion and Celestoderm-V lotion. This is not necessarily expected as it is a well-established fact that the nature of the base affects the release of the active ingredient. Betnovate cream and Celestoderm-V cream show similar blanching activities, whereas Celestoderm-V ointment has a superior activity to that of Betnovate ointment (6). A similar example of the influence of the base has been observed in the case of fluocinolone acetonide (7).

It could be expected, however, that due to the good surface coverage, skin contact and spreadibility of lotions, that the corticosteroid would be released equally well from different lotion bases. □

Acknowledgements

One of us (E.M.) acknowledges the H. Bradlow Scholarship for post-graduate studies.

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