FLUTICASONE PROPIONATE (0.05%) CREAM COMPARED TO BETAMETHASONE VALERATE (0.12%) CREAM IN THE TREATMENT OF STEROID-RESPONSIVE DERMATOSES A MULTICENTRIC STUDY*

Fluticasone propionate is a new topical steroid developed as a result of modification of the 19-carbon androstane structure.In the present study, efficacy of this steroid was compared with betamethasone valerate cream in patients with psoriasis and eczema. Though fluticasone propionate was marginally more effective than betamethasone valerate, this difference was not statistically significant.

Introduction

Topical corticosteroids remain the mainstay of treatment of inflammatory dermatoses. Considerable anxiety prevails about their side effects. The two major side effects are the local effect of skin thinning,[1] and the systemic effects due to suppression of the HPA axis and Cushing's syndrome.[2]

Many attempts have been made with varying degrees of success to discover new derivatives with increased lipid solubility, more selective localized action and relative freedom from systemic side effects by modifications to the 21-carbon pregnane skeleton structure. Recent research has shown that certain halogenated derivatives of androstane possess some of the desired properties. Fluticasone is one such novel synthetic corticosteroid developed as a result of modifications of the 19-carbon androstane structure.

Despite its androstane origin, fluticasone propionate is highly selective for glucocorticoid receptor and has negligible androgenic activity.[3] Its high lipophilicity results in a long half life of 8-12 hours.[4] It has very little propensity for systemic absorption[5] and is metabolised repidly to a metabolite with negligible activity at the steroid receptor.[6] Vasoconstrictor assays in normal volunteers using an alcohol vehicle revealed that fluticasone propionate has vasoconstrictor activity 9.5 times greater than fluocinolone acetonide and intermediate between that of the betamethasone valerate and clobetasol propionate.[7,8]

The objective of our study was to evaluate the clinical efficacy, safety and tolerability of this new steroid in the treatment of eczema and psoriasis and compare it with betamethasone valerate cream. Fluticasone propionate (0.05%) cream and betamethasone valerate (0.12%) cream were evaluated in a multicentric double-blind study randomised within patients who suffered from bilateral, roughly symmetrical, moderate to severe eczema and psoriasis.

Materials and Methods

On inclusion, the various signs and symptoms of the patients were graded

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separately for the left and right sides of the body on a 4-point scale as per criteria given below. Only those patients with a total score of 6 or above were included for the study. In the case of eczema, the inclusion criteria of a score of at least 6 was to be obtained in the first 3 parameters alone.

Criteria for scoring is eczema :

Parameters scored		Criteria
Erythema	)	0-Absent
Exudation	)	1-Mild
Pruritus	)	2-Moderate and
Lichenification	)	3-Severe
Vesiculation and	)	
Crusting	)	

Criteria for scoring in psoriasis :

Parameters scored		Criteria
Erythema	)	0-Absent
Lichenification	)	1-Mild
Pruritus	)	2-Moderate and
Scalig	)	3-Severe

Pregnant and lactating women, patients who had taken systemic steroids in the past 4 weeks or topical steroids in the preceding 2 weeks, patients with hepatic or renal dysfunction or any other clinical condition or concomitant disease that could interfere with the evaluation and children under 12 years were excluded.

Each patient was supplied 2 identical tubes, one containing fluticasone propionate cream (0.05%) and the other betamethasone valerate cream (0.12%). The tubes were distinctly marked by the letter "L" or "R" for treatment of left side or right side of the body. These were packed according to a randomisation code. At the end of each week they reported for follow-up when all the parameters enumerated above were scored again and recorded. Medication for next week's treatment was issued. Treatment was continued for 4 weeks with weekly follow-up visits and evaluation. Every patient was also issued a diary card with clear instructions on the method and quantity of cream application and asked to bring the completed diary card with his treatment preference marked on it on the last day of treatment. Patients were also asked to return any left over medication tubes at the end of every week. Adverse events, if any, reported by the patients and or observed by the investigator were carefully recorded.

The primary end-point for assessment of efficacy was the overall evaluation which was graded in accordance with the following criteria :

Cleared - when 100% resolution occurred

Excellent - when at least 75% reduction in total score was observed

Good - when 50-74% reduction in total score

Poor - when less than 25% reduction in total score and

Worse - if exacerbation of disease occurred.

The physician's and patient's preference for left or right side medication was recorded as secondary end-point and graded according to preference as follows :

Left side definitely better,

Left side slightly better,

No difference detectable,

Right side slightly better and

Right side definitely better.

Both the total score before initiation of treatment and at the end of weekly follow-up visits and the individual scores for each of the parameters were analysed using Wilcoxon's

matched pair signed rank test.

Results

A total of 107 patients completed the study at the 4 centers, 61 suffered from psoriasis and 46 from eczema. The detailed demographic data is given in Table I.

Table I. Baseline demographic profile

No. of patients	
Enrolled	108
Drop-outs	1
Completed	107
Sex distribution	
Males	79
Females	28
Age (years)	
Mean (SEM)	42.20 (3.78)

The basal scores for both fluticasone propionate cream (0.05%) and betamethasone valerate cream (0.12%) are almost identical in all parameters. Both the creams resulted in similar decline in the individual parameters. This was also reflected in the decline of the total scores. Figure 1 shows the decline in total scores over 4 weeks treatment in psoriasis patients. The decline in both the individual and total scores was greater with fluticasone propionate cream than with betamethasone valerate cream. These differences however were not statistically significant.

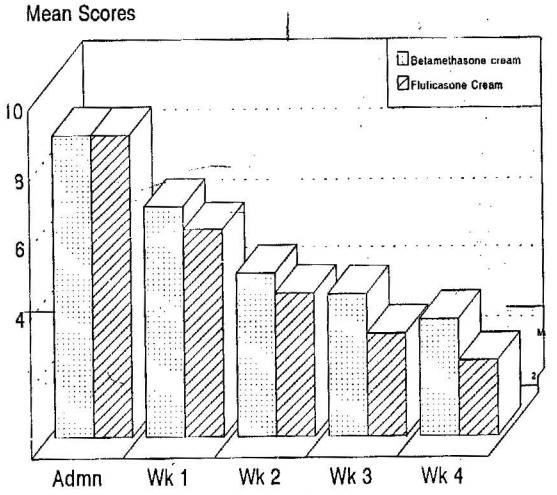

Fig. 1. Pooled data of psoriasis patients (total scores).

Figure 2 shows the decline in total scores over the 4 weeks treatment in patients with eczema. Here again, the basal scores for both fluticasone propionate cream and betamethasone valerate cream were almost identical in all parameters. Both the creams resulted in similar decline in the individual parameters as well as in the total scores. The decline in both the individual and total scores was greater for fluticasone propionate cream treatment than for betamethasone valerate cream treatment. These differences were however not statistically significant.

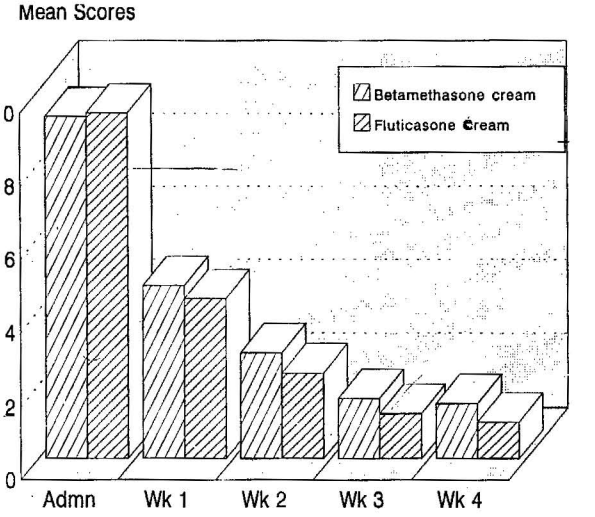

Fig. 2. Pooled data of eczema patients (total scores)

The overall evaluation of treatment in psoriasis and eczema patients is reflected in Figure 3. In both the groups, fluticasone propionate cream had an edge over betamethasone valerate cream in terms of more number of patients being rated as 'Excellent' and 'Good' and less number of poor ratings. Nevertheless the differences did not reach statistical significance.

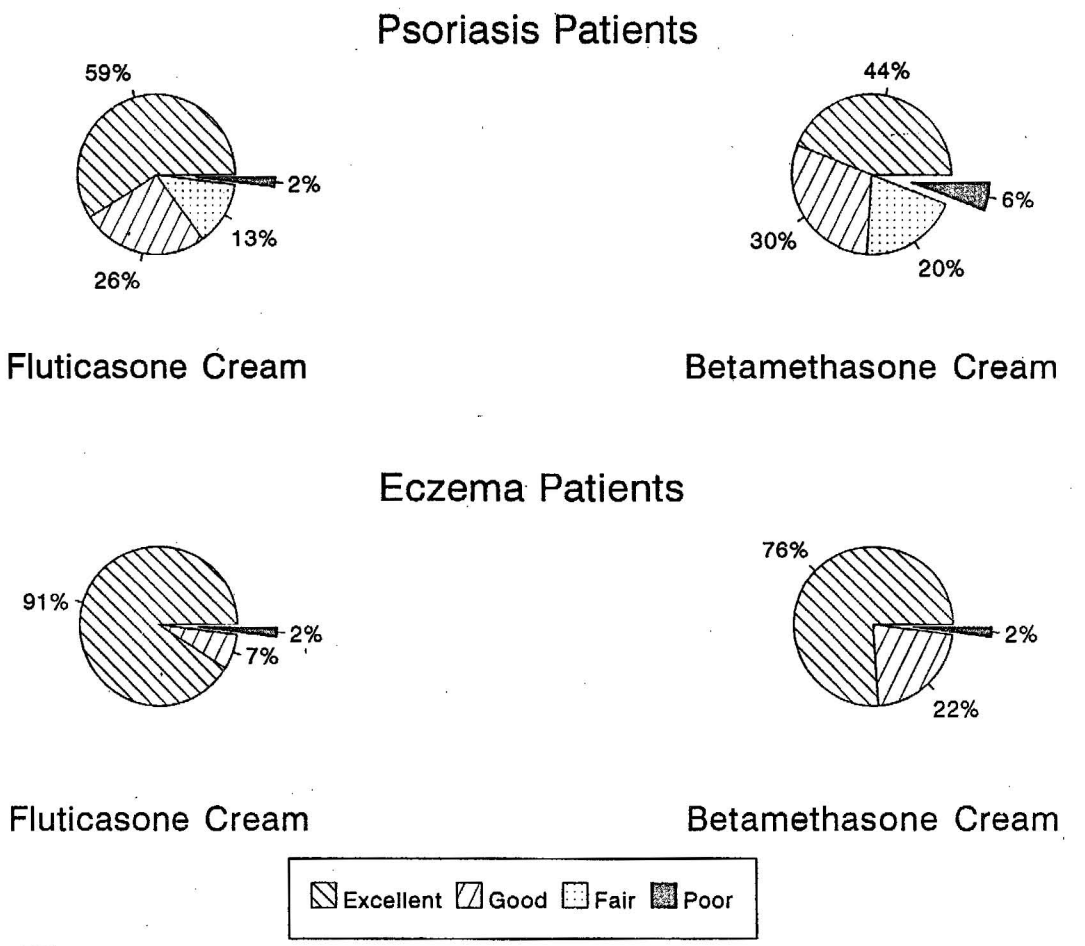

Fig. 3. Overall evaluation in psoriasis and eczema.

Figure 4 reflects the treatment preferences in both psoriasis and eczema groups. Both the investigators and the patients reflected a similar trend with respect to treatment preference. The preference for fluticasone propionate cream in both psoriasis and eczema was greater by 50% or more than that for betamethasone valerate cream both by the investigators and the patients. These differences were also not statistically significant.

While both the creams were well tolerated, following side effects were observed in 5 patients, namely, acne in 2 patients, tiny guttate lesions in 2 patients, and lichenoid eruption in 1 patient. These were mild and self-limiting and did not interfere with the patient's well-being nor was it necessary to discontinue treatment. In all the cases, both sides of the body were affected and it was not possible to attribute the side-effects to a single drug. One patient during first week of treatment developed exacerbation of the lesions on the side on which betamethasone valerate cream was applied. This patient was excluded from efficacy analysis.

Discussion

Fluticasone propionate 0.05% has high affinity and selectivity[3] for the glucocorticoid

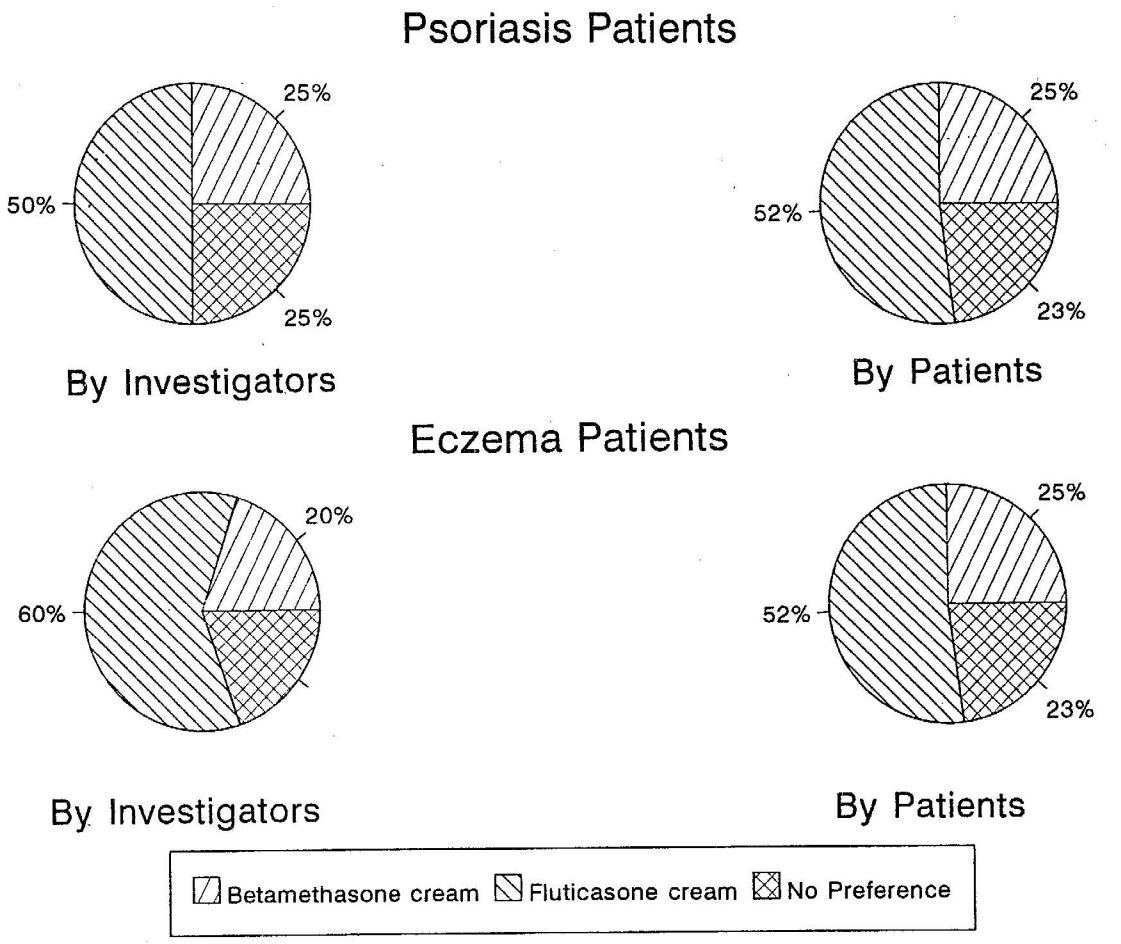

Fig. 4. Treatment preference in psoriasis and eczema.

receptor. This is reflected by a parallel clinical efficacy to betamethasone valerate 0.12%. Besides, it was shown[9] that skin thinning as measured by ultrasound or biopsy was not statistically significant as compared to placebo over 8 weeks of once daily treatment. Any skin thinning that occurred returned to normal baseline values after treatment was stopped. Fluticasone propionate is also devoid of systemic side effect of HPA-axis suppression.[10]

Fluticasone propionate has been found to be as effective as betamethasone-17-valerate cream (0.1%) for treatment of moderate to severe psoriasis.[11] Our experience has been similar.

Multicentric studies in the UK[11] have shown that once-daily application of fluticasone propionate cream 0.05% is equivalent in efficacy to twice-daily treatment with fluticasone propionate cream 0.05% when used over a 4-week treatment period for patients with moderate to severe atopic eczema. This is a very important finding considering the still further reduced potential for side effects, both local and systemic, with just once daily application.

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