Hydrocortisone Butyrate 0.1% Cream in the Treatment of Chronic Dermatitis

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This multicenter, randomized, double-blind clinical trial involving 89 subjects (86 with chronic hand dermatitis and 3 with atopic dermatitis) compared the safety, efficacy, and cosmetic acceptability of 4 medium-potency topical corticosteroid products: hydrocortisone butyrate (HB) 0.1% cream (Locoid Lipocream®), fluticasone propionate (FP) 0.05% cream (Cutivate®), prednicarbate (PC) 0.1% cream (Dermatop®), and mometasone furoate (MF) 0.1% cream (Elocon®). Subjects were randomly assigned to 1 of 3 treatment groups (HB vs FP, HB vs PC, or HB vs MF) and further randomized to HB on the right or the left side, and FP, PC, or MF on the contralateral side. Treatments were self-administered twice daily for 2 weeks. Assessments of efficacy were based on the investigator ratings of signs and the subject ratings of signs and symptoms. Cosmetic acceptability was assessed by direct comparisons between products using a subject questionnaire. The results indicated comparable efficacy of all 4 medium-potency corticosteroid products and suggested that, compared to other corticosteroid creams, the HB vehicle yielded somewhat greater subject preference with respect to cosmetic appeal.

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Topical corticosteroids remain the mainstay of therapy for inflammatory skin conditions such as hand dermatitis and atopic dermatitis.[1,2] The appearance of treatment alternatives involving combinations of corticosteroids with newer immunomodulating agents[3,4] has led to an increase in the demand for a variety of treatment options, including corticosteroids of different potencies and in different vehicles. Use of the various treatment options is highly individualized, based on factors such as extent and severity of the condition, treatment history, patient age, allergic and irritant sensitivity, and cosmetic acceptability. This clinical trial was undertaken to evaluate the safety, efficacy, and cosmetic acceptability of a high-lipid emollient cream formulation of hydrocortisone butyrate (HB) 0.1% (Locoid Lipocream®) as compared with 3 other medium-potency corticosteroid cream products—fluticasone propionate (FP) 0.05% cream (Cutivate®), prednicarbate (PC) emollient 0.1% cream (Dermatop®), and mometasone furoate (MF) 0.1% cream (Elocon®)—in the treatment of chronic atopic and hand dermatitis.

Methods

Subjects—Subjects were included in the study population if they were between 18 and 65 years of age with moderate hand dermatitis or atopic dermatitis that had persisted for at least 2 weeks prior to their entering the study. The study was designed to make unbiased within-subject comparisons of treatment effectiveness; therefore, subjects had to have approximately symmetrical bilateral involvement at the baseline visit. A total of 89 subjects (86 with hand dermatitis and 3 with atopic dermatitis) were randomized to the study. Subjects could not use other medications known to affect dermatitis, including systemic treatments, for one month prior

to the baseline visit or topical corticosteroids for one week prior to the baseline visit.

Study Design—This was a multicenter, randomized, double-blind, controlled clinical trial of 2 weeks' duration. Subjects were randomized in balanced cohorts to 3 parallel-treatment groups, each group receiving a pair of treatments, HB vs FP, HB vs PC, or HB vs MF. All subjects were treated with HB on the right or the left side, and FP, PC, or MF on the contralateral side. At the baseline study visit, subjects were instructed in the use of the study products. Subjects also made their first application of the products under supervision of the clinical staff. For the next 2 weeks, the subjects self-administered the treatments twice daily following written instructions. The instructions

Table 1.

Clinical Assessments of Dermatitis Severity

	Score			
Sign/Symptom	0=None	1=Mild	2=Moderate	3=Severe
Erythema	None	Mild pinkness	Moderate pink to red	Intense redness
Cracking/fissuring	None	A few shallow cracks	Moderate, early fissures	Deep fissures (1 mm)
Scaling	None	Diffuse mild flaking	Moderate, with or without plaques	Thick scaling plaques
Papules/vesicles	None	A few papules/vesicles	Multiple papules/vesicles, contained	Large bullae or widespread papules/vesicles

Table 2.

Percentage of Subjects Showing Improvement in Signs of Dermatitis*†

		Treatment					
		HB vs FP (n=26)		HB vs PC (n=28)		HB vs MF (n=31)	
Sign	Rated by	HB	FP	HB	PC	HB	MF
Erythema	Investigator	31	23	46	46	42	39
	Subject	50	35	46	39	61	52
Cracking/fissuring	Investigator	62	54	43	21	48	42
	Subject	46	50	43	43	48	52
Scaling	Investigator	65	54	43	54	48	48
	Subject	54	54	43	61	48	42
Papules/vesicles	Investigator	27	23	36	36	26	19
	Subject	27	15	21	29	19	10

*HB indicates hydrocortisone butyrate 0.1% cream; FP, fluticasone propionate 0.05% cream; PC, prednicarbate emollient 0.1% cream; MF, mometasone furoate 0.1% cream.

†Individual pairwise comparisons were statistically significant ($P<.05$) only for subject rating of erythema in the HB vs FP group and investigator rating of cracking/fissuring in the HB vs PC group.

Table 3.

Mean Investigator Total Signs Score ± SD*

	Treatment					
	HB vs FP (n=26)		HB vs PC (n=28)		HB vs MF (n=31)	
	HB	FP	HB	PC	HB	MF
Baseline	4.9±1.1	4.8±1.2	5.0±1.3	5.1±1.3	5.1±1.5	5.1±1.7
Final	3.3±2.4	3.7±2.4	3.4±1.3	3.8±1.7	3.6±2.2	3.4±2.3
Change from baseline	−1.6±2.0	−1.2±2.2	−1.6±1.7	−1.3±1.3	−1.5±1.7	−1.7±1.6
Within-treatment *P* value	.0004	.0112	<.0001	<.0001	<.0001	<.0001
Between-treatment *P* value (within group)	.0626		.3493		.5195	

*HB indicates hydrocortisone butyrate 0.1% cream; FP, fluticasone propionate 0.05% cream; PC, prednicarbate emollient 0.1% cream; MF, mometasone furoate 0.1% cream.

included details regarding the application of specifically labeled products (labeled "left" or "right") to the appropriate side of the body using new vinyl gloves at each application to prevent the intermixing of the materials from one side to the other. The medications were dispensed to the subjects in blind-labeled tubes that were clearly marked with the subject's identification number and the word "left" or "right." At the end of the 2-week treatment period, the subjects returned to the study site for a final examination.

Clinical Assessments—As shown in Table 1, at the baseline and final visits, the investigators and the subjects independently rated the severity of typical signs of dermatitis using a 4-point ordinal scale (0=none, 1=mild, 2=moderate, and 3=severe). In addition, the subject rated 2 additional symptoms, pruritus and pain/burning. The total signs score for investigators was calculated by summing the separate signs scores. The total signs and symptoms score for subjects was calculated by summing each patient's signs and symptoms scores. The percentage of hand involvement for hand dermatitis or the size of the target area for atopic dermatitis also was recorded.

Subject Questionnaires—At the final visit, subjects completed a questionnaire in which they compared both study products with respect to which cream felt more soothing upon application, which cream moisturized the skin better, and which cream was preferred overall.

Safety Assessments—Product safety was assessed through the collection and evaluation of adverse events, either observed by the investigator or volunteered by the subjects.

Statistical Analysis—Changes from baseline to final visit for each investigator's signs score and each subject's signs and symptoms score were categorized as "improved," "worsened," or "no change." The distribution of subjects across these 3 categories was then compared between treatments using the McNemar test. The investigator total scores, the subject total scores, and in patients with hand dermatitis, the percentage of hand involvement (palm, dorsum, and combined) were analyzed within treatment group using the *t* test for paired data. The scores and percentages were analyzed between treatment groups using comparisons of changes from baseline derived from the results of the *t* test for paired data. Demographic and background parameters were compared between treatment groups using analysis of variance and χ^2 tests, as appropriate. No statistical tests were performed for the questionnaire responses or the incidence of adverse events.

Results

Subjects—A total of 89 subjects were enrolled in the study; 27 were randomized to the HB versus FP group, 28 to the HB versus PC group, and 34 to the HB versus MF group. The mean overall age of subjects was 46 years old; 52 of the subjects (58%)

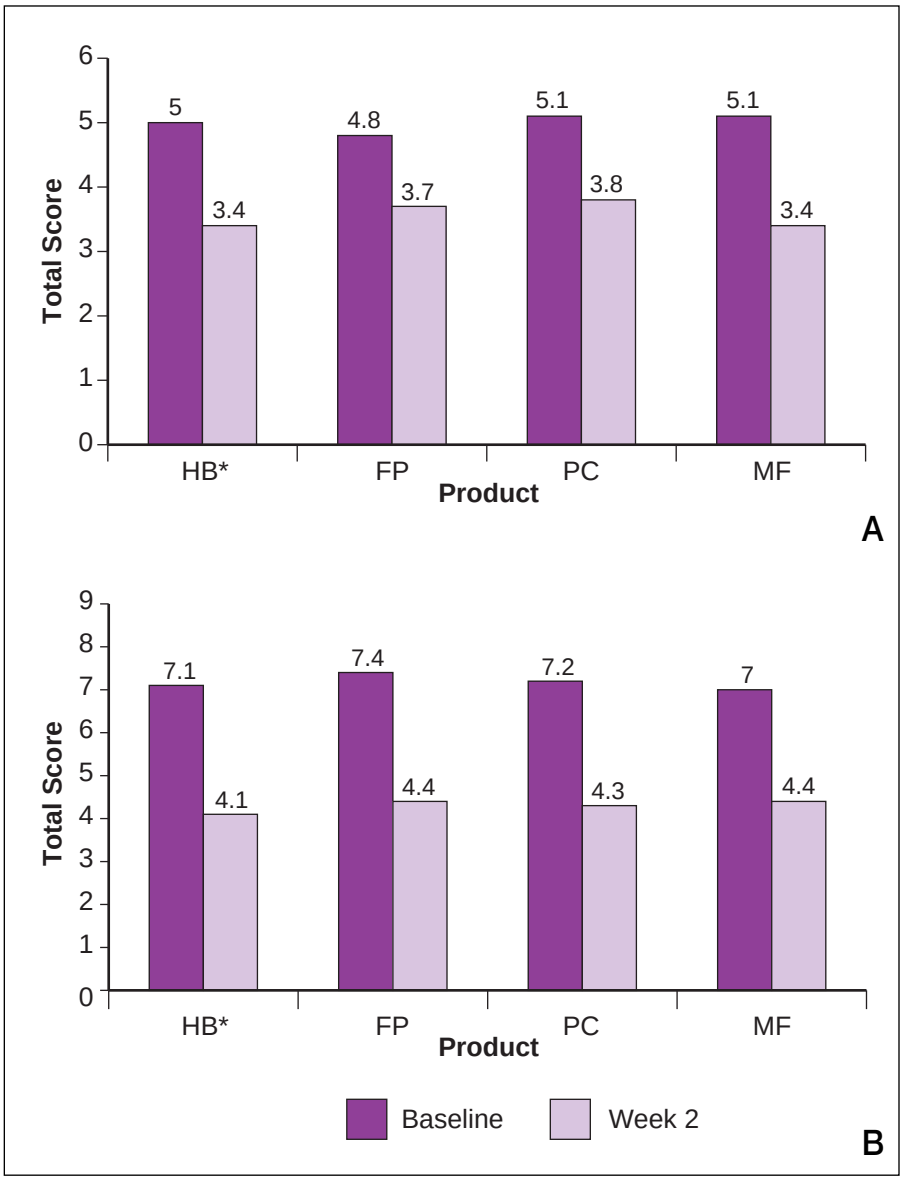

Figure 1. Mean investigator total signs score (A) and mean subject total signs and symptoms score (B). Improvement was statistically significant for all products ($P \leq .011$) between the baseline evaluation and final visit. Asterisk indicates hydrocortisone butyrate mean combines all treatment groups. HB indicates hydrocortisone butyrate 0.1% cream; FP, fluticasone propionate 0.05% cream; PC, prednicarbate emollient 0.1% cream; MF, mometasone furoate 0.1% cream.

were female, and 86 (97%) of the subjects recorded their race as white. The 3 treatment groups (HB vs FP, HB vs PC, and HB vs MF) were very similar with regard to subject age, gender, and race, with no statistically significant differences. Of the 89 enrolled subjects, 86 presented with chronic hand dermatitis and 3 with atopic dermatitis (1 in the HB vs FP group and 2 in the HB vs MF group). The mean duration of dermatitis was 9.1 years in the HB versus FP group, 7.9 years in the HB versus PC group, and 6.9 years in the HB versus MF group; the differences between treatment groups were not statistically significant. Of the 89 randomized subjects, 85 provided complete data at the final visit and were included in the data analyses; 82 of these subjects had hand dermatitis.

Clinical Assessments—The percentage of subjects who exhibited improvement in signs during the 2-week treatment period is shown in Table 2. Based on the investigators' observations, erythema decreased in 23% to 46% of subjects across the different treatment arms, cracking/fissuring decreased in 21% to 62% of subjects, and scaling decreased in 43% to 65%. Statistical analysis showed no differences between the paired treatments within each group in the investigator signs ratings, except that the rate of improvement of cracking/fissuring was statistically greater in the HB group compared with the PC group ($P<.05$). The mean investigator total signs score (Table 3 and Figure 1A) showed significant reductions between the baseline evaluation and final visit for all 4 steroid

Table 4.

Mean Subject Total Signs and Symptoms Score ± SD*

	Treatment					
	HB vs FP (n=26)		HB vs PC (n=28)		HB vs MF (n=31)	
	HB	FP	HB	PC	HB	MF
Baseline	7.0±2.2	7.4±2.1	7.1±3.3	7.2±2.9	7.2±2.8	7.0±3.1
Final	3.8±3.2	4.4±3.5	4.3±3.0	4.3±2.6	4.2±2.9	4.4±3.2
Change from baseline	−3.2±3.9	−3.0±4.0	−2.9±3.3	−3.0±3.2	−3.0±2.7	−2.6±3.2
Within-treatment *P* value	.0003	.0007	.0001	<.0001	<.0001	<.0001
Between-treatment *P* value (within group)	.7572		.8392		.3287	

*HB indicates hydrocortisone butyrate 0.1% cream; FP, fluticasone propionate 0.05% cream; PC, prednicarbate emollient 0.1% cream; MF, mometasone furoate 0.1% cream.

Table 5.

Mean Percentage of Hand Involvement ± SD*

	Treatment					
	HB vs FP (n=25)		HB vs PC (n=28)		HB vs MF (n=29)	
	HB	FP	HB	PC	HB	MF
Baseline	31±25	31±25	42±21	41±20	31±22	32±23
Final	23±21	26±22	33±17	31±17	22±20	23±21
Change from baseline	−8±12	−5±12	−9±15	−10±15	−10±14	−9±15
Within-treatment *P* value	.0014	.0623	.0039	.0016	.0008	.0041
Between-treatment *P* value (within group)	.0866		.5360		.5073	

*HB indicates hydrocortisone butyrate 0.1% cream; FP, fluticasone propionate 0.05% cream; PC, prednicarbate emollient 0.1% cream; MF, mometasone furoate 0.1% cream.

treatments ($P<.02$). The degree of reduction in signs and symptoms was similar for all 4 products, and there were no statistically significant differences between the paired treatments within each group ($P>.06$).

Similar results were observed for the mean subject total signs and symptoms scores (Table 4 and Figure 1B). The mean percentage of hand involvement at baseline ranged from 31% to 42% across the 3 groups (Table 5). After 2 weeks of treatment, these values had declined by 5% to 10%. As with the signs and symptoms scores, the reductions in hand involvement from baseline, although statistically significant for all treatments except FP, showed no evidence of treatment differences between pairs ($P>.08$).

Subject Questionnaires—The responses to the cosmetic acceptability questionnaire (Table 6) showed that the subjects tended to prefer HB to the comparator products for soothing quality and

Table 6.

Percentage of Subjects (n) Preferring Study Product*†

	Treatment								
	HB vs FP			HB vs PC			HB vs MF		
Attribute	HB	FP	n	HB	PC	n	HB	MF	n
Overall	41% (11)	37% (10)	21	54% (15)	18% (5)	20	35% (12)	29% (10)	22
More soothing	30% (8)	19% (5)	13	39% (11)	21% (6)	17	32% (11)	6% (2)	13
Better moisturizing	30% (8)	26% (7)	15	61% (17)	21% (6)	23	38% (13)	15% (5)	18

*HB indicates hydrocortisone butyrate 0.1% cream (Locoid Lipocream®); FP, fluticasone propionate 0.05% cream (Cutivate®); PC, prednicarbate emollient 0.1% cream (Dermatop®); MF, mometasone furoate 0.1% cream (Elocon®).

†Numbers shown reflect all subjects who stated a preference. The remaining subjects stated no preference or omitted response. Percentages apply to all subjects who completed questionnaires.

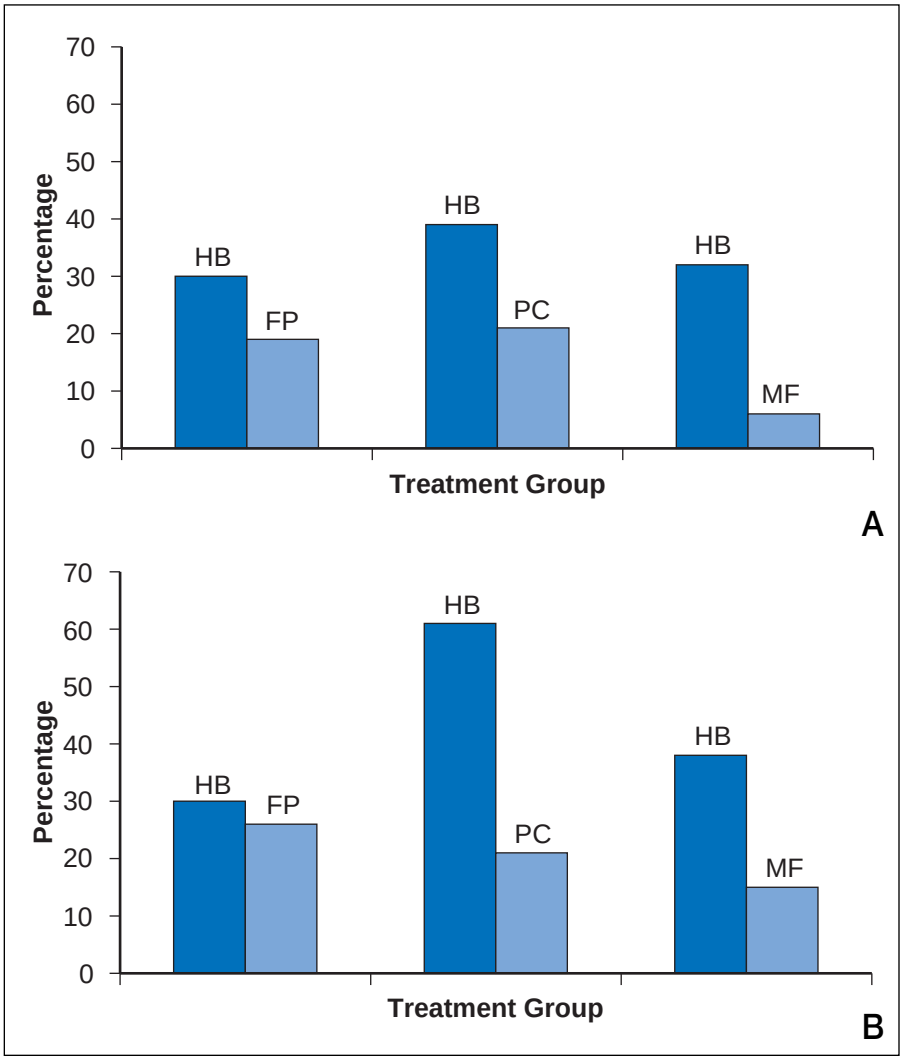

Figure 2. Percentage of subjects preferring study product as "more soothing" (A) and "better moisturizing" (B). HB indicates hydrocortisone butyrate 0.1% cream (Locoid Lipocream®); FP, fluticasone propionate 0.05% cream (Cutivate®); PC, prednicarbate emollient 0.1% cream (Dermatop®); MF, mometasone furoate 0.1% cream (Elocon®).

moisturization. Figure 2 illustrates the results of the questionnaire, with the largest percentage of subjects (61%) preferring HB to PC for better moisturizing.

Safety Assessments—Adverse events occurred in 5 (19%) of 27 subjects in the HB versus FP group, 0 of 28 in the HB versus PC group, and 2 (6%) of 34 in the HB versus MF group. The adverse events that were considered by the investigators to be possibly related to the study treatments were headache and jitteriness (one subject) and mild itching (affecting both sides of one subject in the HB vs FP group). None of the other adverse events were considered by the investigators to be possibly related to the study treatments.

Comment

The results of this study of 89 subjects with chronic dermatitis showed that the 4 medium-potency topical corticosteroid products had comparable efficacy in improving erythema, cracking/fissuring, scaling, papules/vesicles, pruritus, and burning and in reducing the extent of hand involvement in subjects with hand dermatitis. The subjects preferred the HB lipid-rich emollient cream formulation to the other 3 products with respect to its soothing and moisturizing qualities.

HB has been available as a first-line therapy in inflammatory skin conditions since the 1950s. As a nonhalogenated class 5 (medium-potency) corticosteroid, HB has a relatively favorable risk-benefit ratio compared with other agents.[5] The Locoid Lipocream formulation was developed specifically to enhance moisturization, occlusive effect, and cosmetic acceptability for treatment of subacute and chronic dermatoses, especially those with a component of dry skin. The high-lipid formulation is semiocclusive and emollient and contains no propylene glycol or lactic acid, which are mild dermal irritants used as excipients in other corticosteroid creams.[6] Earlier reports have noted the effectiveness and cosmetic acceptability of this product in treating chronic dermatitis.[7-9]

Vehicle characteristics and properties in this class of drug products have therapeutic relevance beyond the delivery of the drug substance to its site of action. Moisturizing creams and emollients are important therapeutic adjuncts in themselves.[10,11] The occlusive properties of ointments help retain moisture, but ointments may be sticky and uncomfortable to use. A vehicle that has favorable cosmetic attributes, is easy to apply, and is pleasant and comfortable to use ensures better compliance to the treatment regimen and consequently, better treatment outcomes.

The current results are the first reported of a direct within-subject comparison of HB with 3 marketed standards of its product class. These results indicate comparable efficacy with other medium-potency corticosteroids. The study results also suggest that the HB vehicle yields somewhat greater subject preference with respect to cosmetic appeal compared with other corticosteroid creams.

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