Evaluating the Efficacy and Safety of Calcipotriene/Betamethasone Ointment Occluded With a Hydrogel Patch: A 6-Week Bilaterally Controlled, Investigator-Blinded Trial

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Occlusive therapy with or without topical agents is effective in the treatment of psoriasis. This study assessed the efficacy and safety of an occlusive hydrogel dressing. Participants were treated with calcipotriene 0.005%–betamethasone dipropionate 0.064% ointment with and without a hydrogel patch. Thirty participants completed the 6-week, bilaterally controlled, investigator-blinded, single-center study. Substantial reductions in total modified psoriasis area and severity index (PASI) scores of occluded lesions versus nonoccluded lesions were seen as early as the first week of treatment and sustained through 4 weeks of the study. No adverse effects related to the study, including skin irritation, were observed or reported. Hydrogel dressings provide an effective and safe occlusive option to enhance topical therapy for psoriasis.

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Psoriasis is a common problem encountered in dermatologic patients, affecting up to 7.5 million Americans and 125 million individuals worldwide.[1] Recent advances most notably involve the advent of biologic therapies for severe generalized psoriasis. However, most psoriatic patients have mild to moderate disease for which topical therapies remain first-line treatment.

It is known that occlusion increases the efficacy of topical agents. However, occlusion with adhesive bandages[2] or plastic wrap[3] is difficult to use and uncomfortable to wear. Plastic wraps lack intrinsic adhesive properties. They also have complications such as risk for tape burn and sweat accumulation underneath the wrap, which may exacerbate disease states. Overall, they tend to be impractical, not user-friendly, and cosmetically inelegant.

To address these limitations, an innovative self-adhesive and hypoallergenic dressing composed of a thin, flexible, flesh-colored hydrogel layer on a gas and water impermeable urethane backing was custom designed for dermatologic use (not yet commercially available). Unlike hydrocolloid dressings, which have low water content, the hydrogel layer is approximately 50% water. It contains no steroids, but the impermeable backing helps to enhance absorption when used in conjunction with topical medications. In addition, the patch has been shown to be effective for psoriasis treatment even when used alone as monotherapy.[4] This patch

will hopefully provide a practical, inexpensive, and aesthetically pleasing self-adhesive occlusive dressing. This study aims to investigate the efficacy and safety of the hydrogel patch when used in combination with calcipotriene 0.005%–betamethasone dipropionate 0.064% ointment.

Methods

This bilaterally controlled, investigator-blinded study was conducted at the University of California, San Francisco, Psoriasis, Phototherapy & Skin Treatment Clinic, between July 2009 and December 2009. The protocol was approved by the institutional review board and participants gave written informed consent before starting study procedures.

Study Design and Treatment—Adult male and female patients with stable plaque-type psoriasis were evaluated for this study. Patients were required to have 2 symmetrical psoriatic lesions that were similar in erythema, induration, and scaling. Based on these 3 parameters as part of the modified psoriasis area and severity index (PASI) scale, plaques were scored on a scale of 0 (no evidence) to 4 (severe appearance) for a maximum score of 12. Target plaques must have had a total modified PASI score of 7 or greater and were within 1 point of each other for each of the 3 parameters. Lesions located on the scalp, face, or genitals were excluded. Patients with evidence of a skin disorder other than plaque-type psoriasis, clinically infected psoriasis, and/or skin atrophy in the area of the target lesions also were excluded. Cessation of topical or intralesional therapies (other than emollients) to target lesions for 2 weeks and investigational drugs or systemic psoriasis therapies for 4 weeks was required prior to starting study procedures.

Study participants were instructed to apply calcipotriene 0.005%–betamethasone dipropionate 0.064% ointment once daily to both psoriatic lesions. One of the 2 lesions was then occluded with a hydrogel patch for at least 6 to 8 hours daily. For psoriasis other than target lesions, study participants were allowed to continue topical regimens instituted prior to study participation.

Assessments—Study participants were evaluated at screening; week 0 (baseline); and during treatment at weeks 1, 2, 3, and 4. After 4 weeks, treatment to target lesions was discontinued for 2 weeks and patients were reassessed at week 6. At each visit, target lesions were photographed and assigned a modified PASI score by a blinded investigator. Each area treated with calcipotriene/betamethasone ointment was assessed for signs of skin atrophy during PASI scoring. Safety was assessed based on the incidence of observed or reported adverse events.

Statistical Analysis—The primary end point was change in total modified PASI score at week 4 compared to baseline. Secondary end points were changes in individual scores for erythema, induration, and scaling at week 4 compared to baseline. All parameters also were compared between weeks 4 and 6 (ie, 2 weeks after treatment discontinuation).

Paired *t* test analysis was utilized to compare these end points. Last observation carried forward was used to impute missing data. Statistical significance was based on $\alpha = .05$.

Results

Participant Disposition and Characteristics—A total of 35 participants were enrolled in the study. Five participants were lost to follow-up prior to study completion. None of the participants discontinued because of lack of efficacy or adverse events. Participant demographics are presented in Table 1.

Efficacy—The total modified PASI score was significantly more improved in the occluded arm compared to the unoccluded arm at the end of the treatment period ($P = .0008$)(Table 2). Substantial improvement was observed as early as week 1 and this difference was maintained through the end

Table 1.

Participant Demographics

	Participants
No. enrolled	35
Mean age, y	46.5
Gender, n (%)	
Male	18 (51.4)
Female	17 (48.6)
Race, n (%)	
White	22 (62.9)
Asian	6 (17.1)
Hispanic	2 (5.7)
Black	2 (5.7)
Other	3 (8.6)

of treatment (Figure 1). Of the individual PASI components, induration and scaling but not erythema (Table 2)(Figure 1) demonstrated statistically significant differences in favor of the occluded arm (P=.0028 and P=.0500, respectively). After discontinuation of treatment, results from both total and individual modified PASI components indicated that occluded lesions recurred at a slower pace than unoccluded lesions, but this difference was not statistically significant (Table 3)(Figure 2).

Safety and Tolerability—No adverse effects related to the study, including skin irritation, were observed or reported. No signs of skin atrophy were noted in any of the participants being followed while on topical therapy.

Comment

The role of occlusive therapy in dermatology is well-known, especially regarding the enhancement of psoriatic treatment regimens. Although the therapeutic mechanism of occlusion is not completely understood, it has been shown to restore defective barrier function and to normalize the epidermal calcium gradient in psoriatic plaques.[5] Studies have demonstrated that occlusion also decreases epidermal mitotic activity in psoriatic plaques[6,7] and increases hydration of the stratum corneum, thereby facilitating desquamation, preventing parakeratosis,[8,9] and restoring the granular layer of the epidermis.[6]

Our study confirms that calcipotriene/betamethasone ointment under occlusion with a hydrogel patch is more effective than ointment

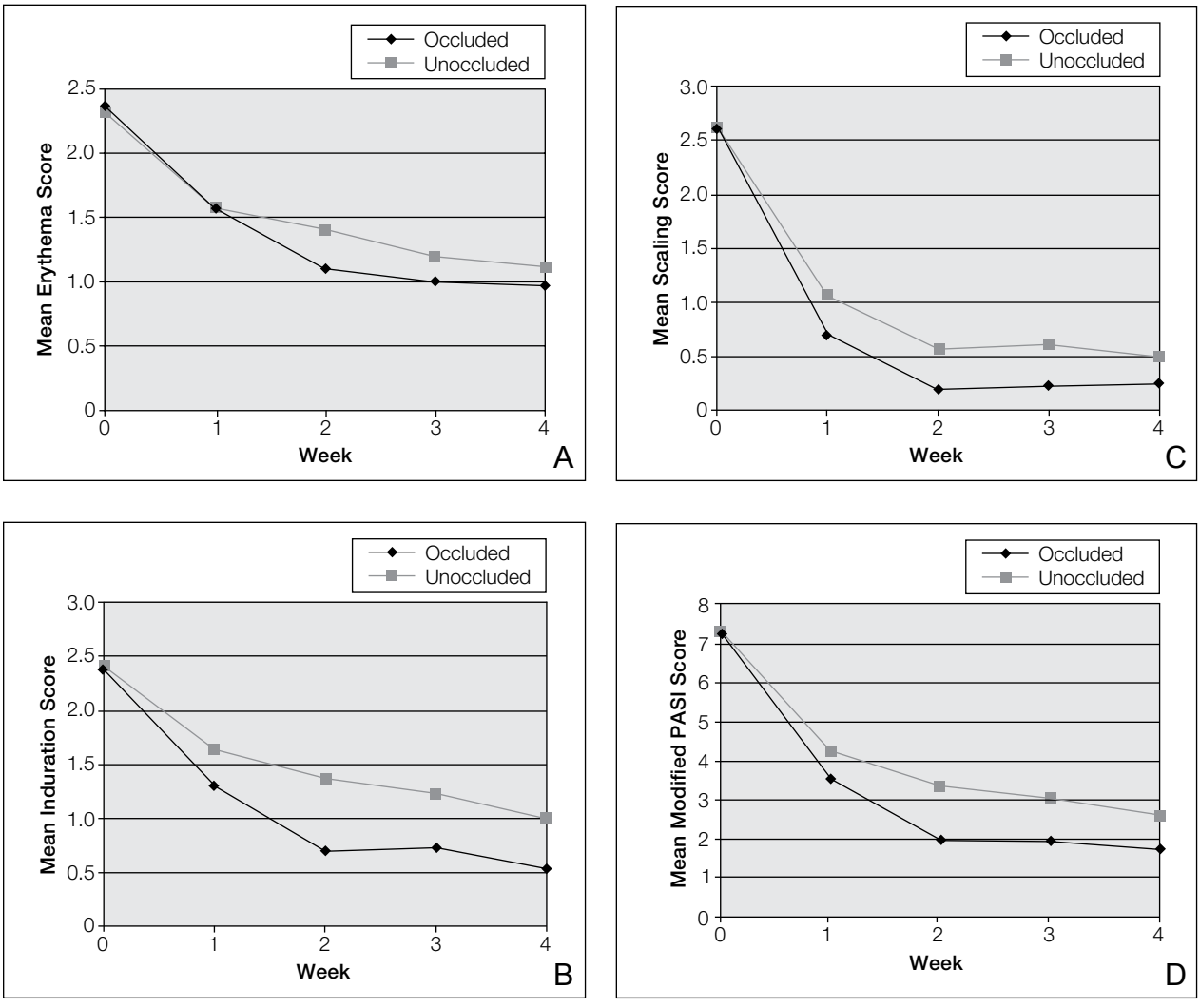

Figure 1. A greater decline in erythema (A), induration (B), scaling (C), and total mean modified psoriasis area and severity index (PASI)(D) scores were observed for occluded treatment areas compared to unoccluded areas. Scored on a scale of 0 (no evidence) to 4 (severe appearance).

Table 2.

Differences in Mean Scores (Week 0 vs Week 4): Treatment Period[a]

	Erythema		Induration		Scaling		Total Modified PASI	
	Occluded	Unoccluded	Occluded	Unoccluded	Occluded	Unoccluded	Occluded	Unoccluded
Mean week 0	2.3438	2.3125	2.3750	2.4063	2.6250	2.6250	7.3438	7.3438
Mean week 4	0.9643	1.1071	0.5357	1.0000	0.2500	0.5000	1.7500	2.6071
Mean difference for week 0 vs week 4 (occluded vs unoccluded)	−0.1786		−0.4286		−0.2500		−0.8571	
P value	.1341		.0028		.0500		.0008	

Abbreviation: PASI, psoriasis area and severity index.
[a]Scored on a scale of 0 (no evidence) to 4 (severe appearance).

Table 3.

Difference in Mean Scores (Week 4 vs Week 6): Posttreatment Follow-up[a]

	Erythema		Induration		Scaling		Total Modified PASI	
	Occluded	Unoccluded	Occluded	Unoccluded	Occluded	Unoccluded	Occluded	Unoccluded
Mean week 4	0.9643	1.1071	0.5357	1.0000	0.2500	0.5000	1.7500	2.6071
Mean week 6	0.8214	1.1071	0.5357	1.1429	0.6429	1.0357	1.9286	3.2857
Mean difference for week 4 vs week 6 (occluded vs unoccluded)	−0.1481		−0.1111		−0.1111		−0.3704	
P value	.2936		.3265		.2646		.1249	

Abbreviation: PASI, psoriasis area and severity index.
[a]Scored on a scale of 0 (no evidence) to 4 (severe appearance).

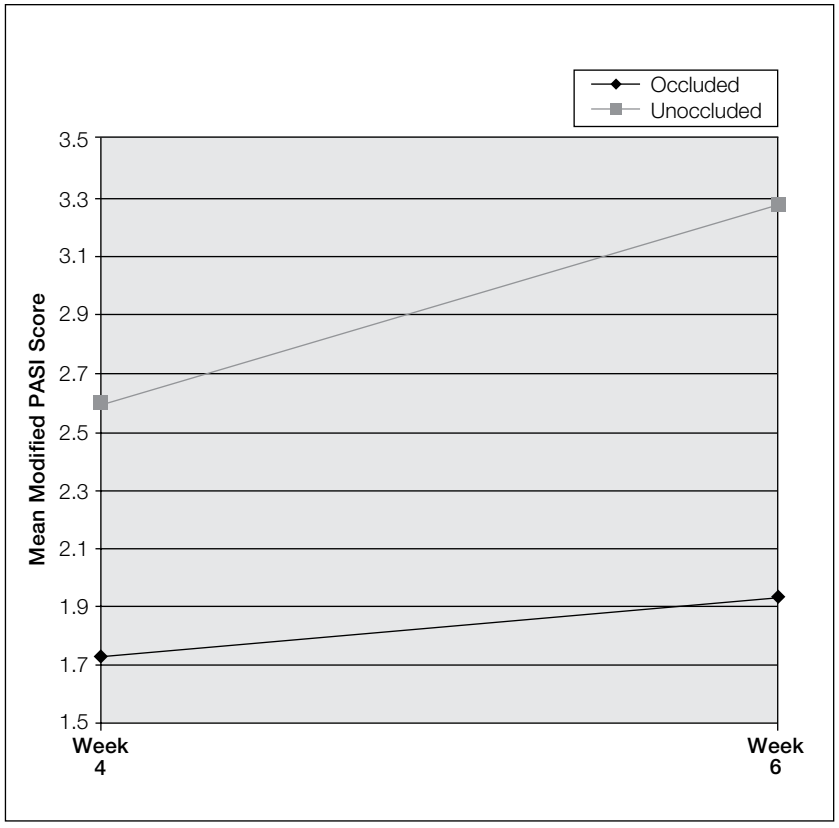

Figure 2. Occluded lesions recurred at a slower pace than unoccluded lesions according to the total mean modified psoriasis area and severity index (PASI). Scored on a scale of 0 (no evidence) to 4 (severe appearance).

alone. Substantial differences were observed in participants as early as the first week of treatment and sustained through 4 weeks of the study, which suggests that patients expecting immediate relief can substantially benefit from this treatment. Prior studies also have confirmed that the hydrogel patch can enhance other topical medications such as triamcinolone acetonide cream 0.01%, calcipotriene cream 0.005%, and tacrolimus ointment 0.1% in the treatment of psoriasis. These studies also demonstrated that the use of the hydrogel patch was effective as monotherapy without the addition of topical agents, though the magnitude of improvement was better with topical agents.[4]

In our study, the use of topical corticosteroids under hydrogel occlusion did not cause any local adverse events such as irritation, skin atrophy, telangiectases, or striae. Nonetheless, it is important to monitor patients closely for signs of skin atrophy and other cutaneous side effects when topical corticosteroids are used under occlusion.[4] Other studies reported rare localized irritation with the hydrogel dressing in conjunction with calcipotriene, a medication that is known to have a higher incidence of irritation than topical corticosteroids.[10] However, the presence of a topical steroid in our study medication may have prevented this potential irritation. Finally, although it was not observed in this study, the Köbner phenomenon has been observed with the use and removal of hydrocolloid dressings.[11-13] In contrast, with hydrogel patches, Köbner phenomenon was not observed in this study or prior studies.[4]

As a strategy to enhance topical therapy for recalcitrant lesions, the potential applications of the hydrogel dressing are endless because of its ability to enhance the efficacy of topical medications. Other skin conditions such as lichen simplex chronicus or prurigo nodularis are logical candidates for future studies.[4] Furthermore, the dressing may act as a physical barrier to discourage patients from excoriating skin lesions. Future possibilities include formulating the hydrogel dressing with topical agents to further simplify therapy and encouraging patient compliance, similar to the lidocaine impregnated hydrogel patch (lidocaine patch 5%).

Conclusion

This study and prior studies demonstrate that the hydrogel dressing can be safely used not only as monotherapy but also as an occlusive device to enhance the efficacy of topical medications in the treatment of psoriasis. Further studies should be undertaken

to examine the effect of hydrogel dressing occlusion on the relapse rate of psoriasis and its use in other dermatoses.

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