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The Role of Clobetasol Propionate Emollient 0.05% in the Treatment of Patients with Dry, Scaly, Corticosteroid-Responsive Dermatoses

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Objective

To provide an overview of the characteristics of the high-potency corticosteroid clobetasol propionate; examine the rationale for combining clobetasol propionate with an emollient; and summarize the safety and efficacy results of recent studies of clobetasol propionate emollient cream 0.05%.

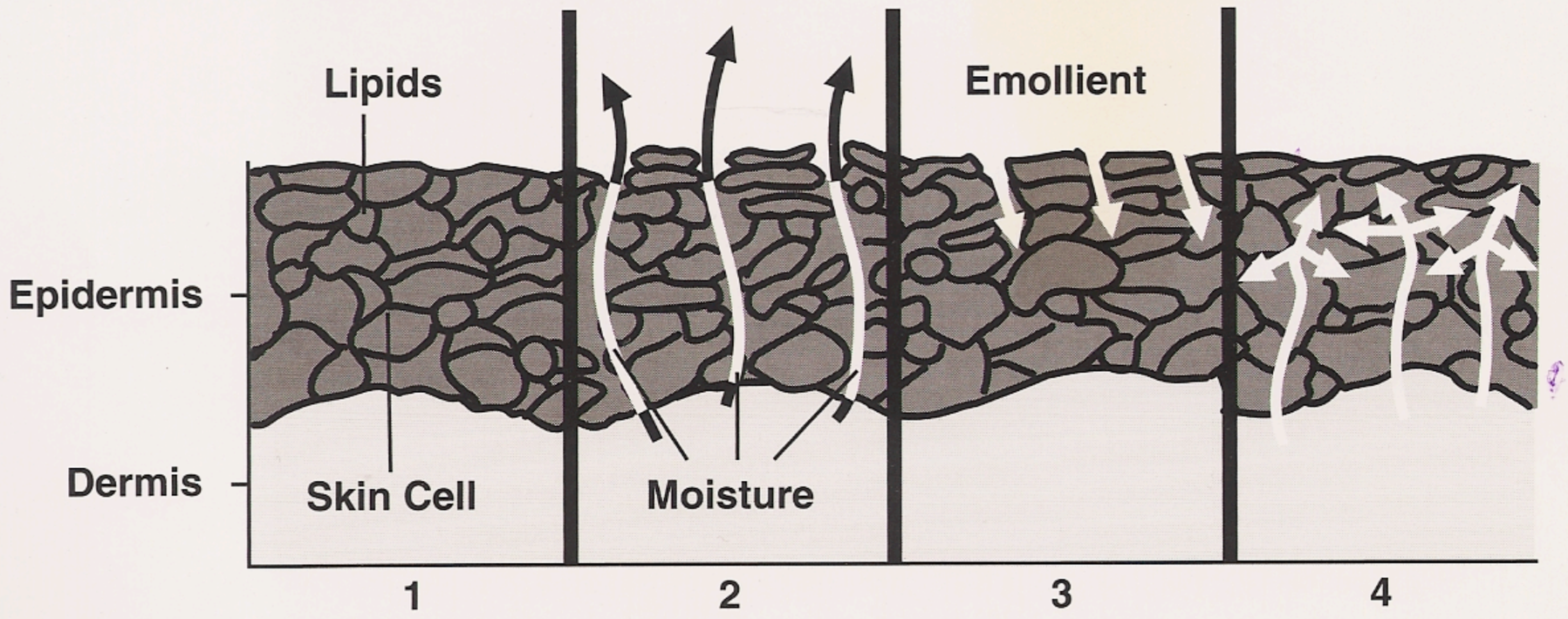
Key points

1. **The treatment of a dry skin condition along with the disease state may enhance the overall clinical improvement.**
   - Dry skin may contribute to a progressively worsening cycle in dermatological conditions
   - Inability of the skin to retain water leads to further drying, exacerbating itching
   - One goal in the management of dry skin conditions is to moisturize the skin to reduce dryness and its associated itching and scratching

2. **The use of an emollient (although not an active ingredient in a steroid) can help restore the skin's normal moisturizing process.**
   - Application of an emollient helps restore intercellular lipids, improving water retention and interrupting the dry skin cycle
   - Dimethicone, contained in the emollient formulation of clobetasol propionate, has the ability to penetrate crevices to form a plastic-like barrier
   - Humectants in the emollient formulation attract and hold water within the skin, reducing transepidermal water loss

3. **Clobetasol propionate emollient 0.05% is a super-high potency [Class I] corticosteroid that contains dimethicone and two emollients to help treat corticosteroid-responsive dermatoses.**
   - The emollient corticosteroid formulation provides fast onset and continued relief
   - Clobetasol propionate is available in an emollient cream, gel, cream, ointment, and scalp application (each contain 0.05% of steroid)

The moisturizing process



From Jackson EM.[1]

1. Spheres correspond to intercellular lipids in intact skin. 2. Moisture from dermoepidermal junction diffuses up and through dry, cracked skin. 3. Emollients penetrate the stratum corneum to restore barrier function. 4. Moisture diffuses up from the dermoepidermal junction to become entrapped in intercellular lipids, which redistribute the moisture throughout the stratum corneum.

Efficacy and safety

Several clinical trials designed to evaluate the safety and efficacy of the emollient formulation of clobetasol propionate support its use in the treatment of a variety of conditions, including:

Plaque-type psoriasis

- A total of 89 outpatients with moderate-to-severe plaque-type psoriasis were randomized to receive either clobetasol emollient cream or vehicle twice daily for 4 consecutive weeks
- Clobetasol emollient showed significantly greater improvement *vs* vehicle for total signs/symptoms and scaling by Day 4, erythema and skin thickening by Day 8, and pruritus by Day 15 $P \leq 0.006$
- No difference between groups was observed in the incidence of subnormal serum cortisol concentrations
- "Drug-related adverse events (mild to moderate) were reported by five patients (11%) in each treatment group; 9% had burning/stinging, which resolved upon discontinuation of treatment."
- In plaque-type psoriasis, application should be limited to 10% of body surface area.

Atopic dermatitis

- In a double-masked, parallel-group, multicenter trial, 81 patients with moderate-to-severe atopic dermatitis were randomized to receive either clobetasol emollient cream or vehicle twice daily for 4 weeks
- Clobetasol emollient produced significantly greater improvement $P \leq 0.006$ than vehicle in scores for total signs/symptoms at Day 4 and continuing through the rest of the 4-week treatment and posttreatment phases
- None of the patients in the clobetasol group withdrew because of treatment failure
- Drug-related adverse events were reported in one patient in the clobetasol emollient group (pruritus, burning/stinging) and two patients in the vehicle group (skin atropy in one patient and pruritus in the other); none of these events were considered serious.
- The total dosage should not exceed 50 g per week because of the potential for TEMOVATE E to suppress the HPA axis.

Conclusions

1. "In its emollient formulation, clobetasol propionate may help soothe dry skin associated with various dermatologic conditions and contribute to improved clinical results."
2. Recently, there has been increased awareness of "the potential benefits of emollient use in the management of dry skin conditions."
3. "Recent studies in the use of clobetasol emollient suggest that it is safe and efficaceous in the treatment of plaque-type psoriasis in courses up to 4 weeks and that improvements in signs and symptoms can continue for 2 weeks beyond discontinuation of treatment."

Reference: 1. Jackson EM. Moisturizers of today. *J Toxicol Cutaneous Ocul Toxicol.* 1992;11:173-184.

Please see complete Prescribing Information on back cover.

Gordon reprint followed by complete prescribing information for TEMOVATE E®

(clobetasol propionate emollient cream)

Emollient, 0.05%

The Role of Clobetasol Propionate Emollient 0.05% in the Treatment of Patients with Dry, Scaly, Corticosteroid-Responsive Dermatoses

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ABSTRACT

The use of topical corticosteroids has significantly enhanced the treatment of patients with dermatoses such as psoriasis and eczema. In particular, group I high-potency corticosteroids such as clobetasol propionate have proved safe and effective for limited-course treatment of inflammatory and pruritic manifestations of moderate-to-severe corticosteroid-responsive dermatoses. At the same time, much effort has gone into devising more effective strategies for addressing the dry skin conditions associated with various dermatologic disorders. An emollient added to a steroid, although not itself an active ingredient, can help restore the normal moisturizing process of the skin; this may be particularly important in soothing the discomfort of the dry skin conditions often encountered in moderate-to-severe dermatoses. In addition, the degree of epidermal hydration can affect the penetration of steroids into the skin. Therefore, successful outcomes in the treatment of patients with corticosteroid-responsive dermatoses may involve more than use of an effective topical steroid. This article examines a currently available cream formulation of 0.05% clobetasol propionate containing moisturizers—emollients, dimethicone, and a humectant—that may contribute to improved moisture content in treated skin. A review of recent studies shows that clobetasol propionate emollient cream is well tolerated and effective in courses of up to 4 weeks for the treatment of patients with psoriasis or atopic dermatitis. ***Key words:*** clobetasol propionate, emollient, topical corticosteroids, psoriasis, eczema.

INTRODUCTION

Dermatoses associated with dry, scaly, crusted, or erythematous skin continue to consume considerable economic and medical resources. For instance, psoriasis accounts for almost 5% of office visits made for dermatologic reasons, making it the

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third most common dermatologic complaint after warts and acne.[1] Nonspecific eczema accounted for more than 3.3 million office visits in the United States in 1995, and a recent European study documented a greater than 15% frequency of atopic dermatitis in school children.[2,3] Far from being merely an annoyance, moderate-to-severe skin diseases can markedly impair patients' quality of life.[4] Fortunately, the introduction of topical corticosteroids has greatly aided the management of many dermatoses.

A key development in topical steroid therapy was the introduction in 1951 of hydrocortisone for the treatment of patients with inflammatory diseases of the skin, including atopic dermatitis and other eczematous eruptions.[5] Since that time, several increasingly potent synthetic topical glucocorticoids have become available to dermatologists, while research has led to the concomitant development of vehicles that enhance the activity of given glucocorticoids.[6] Corticosteroid formulations have been ranked according to their potency, with the weakest (including hydrocortisone) in group VII and the most potent in group I.[7]

High-potency corticosteroids appear to bind more effectively to glucocorticoid receptors on skin cells and may have other therapeutic activities that are not clearly understood.[7] Like all glucocorticoids, they pass freely through cellular membranes and induce immediate vasoconstriction in vascular tissue, preventing mobilization of polymorphic nucleocytes and monocytes to and at the site of inflammation.[8] Their anti-inflammatory potency has been linked to clinical efficacy when used for controlled periods in specific populations of patients with such dermatoses as psoriasis and eczema.[9]

There are several safety concerns with the use of high-potency corticosteroids. Side effects can include suppression of the hypothalamic-pituitary-adrenal (HPA) axis, skin atrophy, acne, and purpura. High-potency corticosteroids should not be used to treat young children (ie, those <12 years old) because of possible pronounced HPA axis suppression. In adults, side effects can be avoided or reversed by exercising appropriate caution and observing certain guidelines, including restricting the use of cream or ointment containing a 0.05% concentration of high-potency corticosteroid to short courses of treatment, restricting weekly dosage to a maximum of 50 g, and avoiding use on the face, axillae, perianal region, or genitalia.[7,9] Because of the consistent effectiveness of twice-daily, once-daily, and individually titrated dosages of cream or ointment containing 0.05% high-potency corticosteroid and because of the low incidence and severity of side effects when these agents are used properly, high-potency corticosteroids such as clobetasol propionate are likely to be of value in dermatologic therapy for some time to come.[7,9,10] This paper discusses the characteristics of the high-potency corticosteroid clobetasol propionate, examines the rationale for combining clobetasol propionate with an emollient, and summarizes recent studies of the tolerability and efficacy of the cream formulation of 0.05% clobetasol propionate.

OVERVIEW OF CLOBETASOL PROPIONATE

Clobetasol propionate is a super-high-potency dihalogenated corticosteroid that has been marketed since 1973 for short-term topical treatment of the inflamma-

tory and pruritic manifestations of moderate-to-severe corticosteroid-responsive dermatoses.[10] It is available in a cream, an ointment, a scalp application, and, more recently, an emollient cream, each containing 0.05% (0.5 mg/g) of steroid. As measured by the vasoconstrictor assay, clobetasol propionate is more than 1800 times more potent than hydrocortisone.[11] Although topical clobetasol propionate is usually applied to lesions twice daily for 2 weeks, longer treatment periods may be indicated in some patients with recalcitrant conditions. A number of controlled clinical studies of clobetasol propionate have demonstrated its favorable safety profile and efficacy in the treatment of patients with psoriasis,[11–15] eczema,[15] atopic dermatitis,[16] and other corticosteroid-responsive inflammatory dermatoses.[17] In comparisons with other topical corticosteroids (including betamethasone dipropionate 0.5% ointment, halcinonide 0.1% cream, and fluocinonide 0.05% cream), clobetasol propionate produced significantly greater improvements.[11,12,15] Clobetasol propionate was also associated with greater efficacy, as measured by the degree, rate, and duration of healing.[12]

CLOBETASOL PROPIONATE 0.05% EMOLLIENT CREAM: HIGH-POTENCY STEROID PLUS EMOLLIENT

Clobetasol propionate is available in a 0.05% emollient cream formulation that is intended to be more moisturizing and cosmetically pleasing to patients than the standard cream and ointment formulations. The ingredients of this formulation are listed in Table I.[18] Clobetasol propionate 0.05% emollient cream is the only commercially available group I high-potency corticosteroid with a specially formulated moisturizing vehicle that contains two emollients (cetostearyl alcohol and isopropyl myristate), dimethicone to occlude and protect the skin, and a humectant to hydrate and attract water to the skin. The effects of these additives—emollients, dimethicone, and humectant—are discussed later in the article. Since fragrance is a leading cause of contact and cosmetic dermatitis and may aggravate existing dermatoses, the lack of fragrance in clobetasol propionate 0.05% emollient cream may help reduce the potential for skin sensitization or exacerbation of diseased skin.[18–20]

Table I. Ingredients in clobetasol propionate 0.05% emollient cream.

Active drug: Clobetasol propionate	
Ingredient	Function
Cetostearyl alcohol	Stiffening agent
Cetomacrogol 1000	Emulsifying agent
Isopropyl myristate	Solvent, emollient
Propylene glycol	Humectant, solvent
Dimethicone 360	Skin protectant, emollient, skin conditioner
Citric acid	Acidifying agent, buffering agent
Sodium citrate	Buffering agent
Imidurea	Preservative
Purified water	Solvent

Several clinical trials have been conducted to evaluate the properties of the emollient formulation of clobetasol propionate.[16,21] A Phase I vasoconstriction assay in healthy volunteers demonstrated that the emollient cream has a pharmacodynamic effect equivalent to that of the existing cream formulation.[18] Additionally, a crossover study in 12 patients with psoriasis or eczema demonstrated that the emollient formulation had effects on the HPA axis similar to those produced by clobetasol cream, as measured by morning serum cortisol concentrations and response to cosyntropin stimulation.[21] The patients in this study were hospitalized, were ≥18 years of age, had baseline serum cortisol concentrations ≥10 μg/dL, and had either generalized psoriasis or eczema involving at least 30% of the body surface. Lesions were treated twice daily for 7 consecutive days with 1.5 g of the emollient cream formulation of 0.05% clobetasol propionate. Opposite sides of the body were treated during each 7-day period, separated by a 2-week nontreatment washout period. A follow-up evaluation was conducted 1 week after the end of treatment. Baseline morning serum cortisol measurements were obtained on days 1 and 23, and adrenal suppression was measured by serum cortisol response 60 minutes after intramuscular injection of 0.25 mg cosyntropin on days 2, 5, and 9 of the first treatment period and days 24, 27, and 31 of the second treatment period. With the emollient cream formulation of 0.05% clobetasol propionate, only one patient had a serum cortisol concentration <10 μg/100 mL, compared with four patients receiving the same dosage of the standard cream formulation of 0.05% clobetasol propionate. The results suggest that when administered twice daily for 1 week, the emollient cream formulation of 0.05% clobetasol propionate produces similar or less HPA axis suppression than is produced by the standard cream formulation of 0.05% clobetasol propionate.[19]

TWO RATIONALES FOR COMBINING CLOBETASOL WITH AN EMOLLIENT

Emollients Alleviate Dryness Associated with Diseased Skin

The first rationale for combining clobetasol propionate with a moisturizer that includes an emollient, dimethicone, and a humectant is that treatment of a dry skin condition may contribute to overall clinical improvement. Dry skin may contribute to a progressively worsening cycle in dermatologic conditions. For example, in patients with atopic dermatitis, the skin has diminished water-binding capacity, higher transepidermal water loss, and decreased water content compared with normal skin.[22] The inability of the skin to retain water leads to further drying, which exacerbates itching. Subsequent rubbing and scratching cause many of the clinical changes observed in the skin of patients with atopic dermatitis. Therefore, one goal in managing patients with atopic dermatitis and other dry skin conditions is to moisturize the skin to reduce dryness and the associated itching and scratching.[23]

The growing emphasis on preventive medicine is changing the focus of dermatology, causing an increased interest in the medical and psychological benefits of the use of skin care products, including moisturizers and emollients.[19,24] In recognition of the negative impact of dry skin on certain dermatologic conditions, recent consensus guidelines from the American

Academy of Dermatology[25] recommend that although management must be individualized to decrease itching and scratching, appropriate use of emollients can help patients with atopic dermatitis function in a normal, productive manner. Moisturizers can help restore the normal moisturizing process in skin.[25] They may be particularly useful in soothing dry skin conditions such as scaling, dryness, roughness, and other cosmetic conditions associated with dermatoses.[26]

Moisturizers are emulsions, or combinations of oil and water, predominantly of the oil-in-water type.[24] All moisturizers are made of water, lipids, emulsifiers, special ingredients, and preservatives.[27] Special ingredients may include glycerin, urea, dimethicone, allantoin, vitamin E,[27] and emollients such as isopropyl myristate (Table II).

Emollients are topical agents designed to smooth and soften the stratum corneum (figure). They are particularly useful in improving the cosmetic aspects of dermatologic conditions characterized by excessive drying or accumulation of stratum corneum.[27] When the stratum corneum barrier is injured or compromised, as in psoriasis or eczema, transepidermal water loss occurs. Emollients help to restore intercellular lipids, improving water retention and interrupting the dry skin cycle.

In general, the effectiveness of an emollient increases with its degree of occlusiveness.[28] Occlusiveness is an emollient's ability to create a barrier that keeps moisture from leaving the skin. Agents that have occlusive properties (many of which have emollient properties as well) include petrolatum, oils of vegetable and animal origin, glycerin, and fluid silicone or dimethicone.[27,29] The cosmetic moisturizing vehicle in the emollient formulation of clobetasol propionate contains dimethicone, a nontoxic, skin-adherent,

Table II. Ingredients found in moisturizers.

Ingredient	Purpose
Water (one phase of emulsion)	This provides solvent for hydrophilic ingredients.
Lipids (other phase of emulsion)	Lipids used in emollients include mineral oil, petrolatum, lanolin, fatty acids and fatty alcohols, esters such as isopropyl myristate and isopropyl palmitate, and ceramides. These provide solvent for hydrophilic or lipophilic ingredients.
Emulsifiers	Common emulsifiers include soap (formed in situ from other components) and surfactants. These hold the emulsion together.
Special ingredients	Ingredients such as glycerin, urea, dimethicone, allantoin, vitamin E, and aloe add desirable properties such as humectancy, pleasant feel on skin, emollient effects, or a light debriding effect (allantoin); they may provide cosmetic appeal.
Preservatives	The most commonly used combinations include the parabens and a formaldehyde donor. These prevent bacterial and fungal contamination, but pose a potential risk for sensitization in patients with cosmetic dermatitis.

Adapted from Jackson EM.[27]

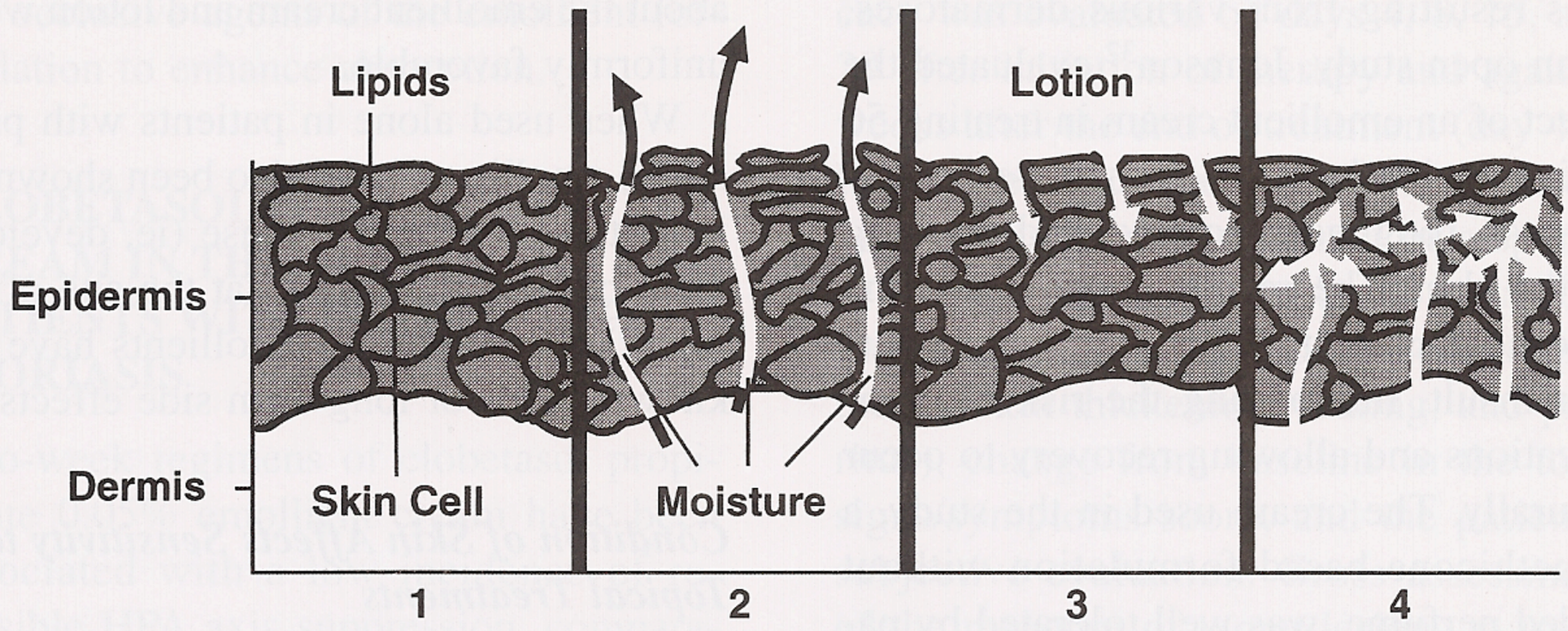

Figure. The moisturization process. 1. Spheres correspond to intercellular lipids in intact skin. 2. Moisture from dermoepidermal junction diffuses up and through dry, cracked skin. 3. Emollients penetrate the stratum corneum to restore barrier function. 4. Moisture diffuses up from the dermoepidermal junction to become entrapped in intercellular lipids, which redistribute the moisture throughout the stratum corneum. Reprinted with permission from Jackson EM.[20]

water-repellent fluid silicone that is both a protectant and an emollient.[18,30] When applied to the skin, its extremely low surface tension allows it to penetrate crevices to form a "plastic" barrier.[18] This emollient base also contains a humectant to help hydrate and attract water to the skin.

Although moisturizers have been used since the beginning of Western medicine and have been available to the public since the 1920s, their physiologic effects were not well understood until the 1980s.[28] Recent scientific and clinical studies have revealed a clear four-step physiologic moisturization process. First, an agent such as dimethicone restores the skin's natural barrier properties to prevent water from leaving the skin through a compromised stratum corneum. Next, the surface cutaneous partition coefficient is altered by ingredients such as humectants that trap and hold water. Then, moisture diffuses across the dermal-epidermal junction. Finally, intercellular lipids are restored, with the result that they can resume their normal function of retaining and redistributing moisture throughout the epidermis.[20,27]

Although the popular understanding of moisturizers is that they work from the top down by infusing moisture into the skin, they in fact work by restoring skin structure and function so that it is moisturized from the bottom up. Most moisturizing products are composed primarily of water (approximately 65% to 85%), which functions as a solvent for hydrophilic moisturizing ingredients. The water evaporates during and shortly after application, leaving behind lipid components that help restore the skin moisture content. Emollient creams contain more oil and less water than other creams and lotions but have less oil than an ointment (Table II).[27,31]

Several clinical studies have examined the effects of treating patients with dry-

ness resulting from various dermatoses. In an open study, Johnson[32] evaluated the effect of an emollient cream in treating 56 patients with dermatoses characterized by dryness, roughness, scaling, and cracking of the skin. The results showed that the emollient protected the skin against further insult, minimizing the risk of complications and allowing recovery to occur naturally. The cream used in the study, a dimethicone-based formulation without added perfume, was well tolerated by patients with dermatitis.

In a 28-day study, Watsky and colleagues[26] demonstrated the advantages of adjunctive emollient therapy in the treatment of 96 patients with stable, chronic plaque-type psoriasis. In the first part of this study, a high-potency topical steroid cream applied twice daily to one test site was compared with a combination steroid cream and emollient applied once daily to a second site in a symmetric location. In the second phase, once-daily application of the steroid was compared with once-daily application of the combination. The results showed that once-daily application of the topical corticosteroid with an added emollient produced significantly more improvement than once-daily application of the topical steroid alone ($P = 0.05$). In fact, once-daily application of the corticosteroid plus emollient was as effective as twice-daily application of corticosteroid cream alone ($P = 0.05$).[26]

In addition, this study demonstrated that once-daily application of both the steroid cream to one site and the combination to a second site resulted in steady improvement in all clinical signs and symptoms and in psoriasis grade. However, at every evaluation interval, the site treated with the combination exhibited a greater degree of improvement. Subjective reports about the emollient cream and lotion were uniformly favorable.

When used alone in patients with psoriasis, emollients have also been shown to inhibit the Köbner response (ie, development of psoriatic lesions at the site of an injury).[33] In addition, emollients have no known short- or long-term side effects.[26]

Condition of Skin Affects Sensitivity to Topical Treatments

A second rationale for combining clobetasol propionate with an emollient is that the cosmetic treatment may enhance delivery and activity of the steroid. Epidermal characteristics such as degree of thickness, presence or absence of fissures, and amount of hydration can affect the activity and penetration of corticosteroids. Increased epidermal thickness caused by hypertrophic disease states can limit penetration of topical corticosteroids, whereas a fissured epidermis permits rapid penetration.[7,8] The degree of epidermal hydration can directly affect the penetration of steroids through the skin.[7,8] More occlusive vehicles increase hydration and therefore enhance penetration of corticosteroids.[7,8] The moisturizing, humectant, and occlusive components of an emollient cream may thus enhance penetration by improving hydration.

In a study comparing the absorption of clobetasol propionate from ointment and cream formulations, a greater amount of steroid was absorbed from the ointment (32.3 vs 23.1 ng/mL per hour), which is more occlusive than the cream.[34] No studies have yet been published comparing the absorption of steroid from the standard formulation of 0.05% clobetasol propionate with that from the emollient formulation or confirming the potential of

the occlusive agents of the emollient formulation to enhance absorption.

CLOBETASOL EMOLLIENT CREAM IN THE TREATMENT OF PATIENTS WITH PLAQUE-TYPE PSORIASIS

Two-week regimens of clobetasol propionate 0.05% emollient cream have been associated with a low incidence of reversible HPA axis suppression, comparable to that produced by the standard cream and ointment formulations.[16] Because some patients may require longer periods of treatment with high-potency topical corticosteroids, information on the HPA axis effects of this formulation for periods longer than 2 weeks is of potential clinical importance. A Phase III randomized, double-masked, parallel-group, multicenter study was conducted to compare the clinical safety and efficacy of clobetasol emollient cream with those of the vehicle alone over a period of 4 weeks, with follow-up at day 43, as reported by Jorizzo et al.[21] A total of 89 outpatients with moderate-to-severe plaque-type psoriasis were randomized to receive twice-daily treatment with either emollient cream (n = 44) or vehicle (n = 45) for 4 consecutive weeks. Eligible patients were nonhospitalized males or nonpregnant, nonlactating females ≥12 years of age with a baseline morning serum cortisol concentration of 5 to 18 μg/dL. A total of 35 patients using clobetasol emollient cream and 39 using vehicle completed the study.

Patients were instructed to apply a thin film of study medication to target lesions twice daily, once in the morning and once in the evening, equaling approximately 0.50 g/d in males and 0.43 g/d in females (not to exceed a total of 50 g/wk). Efficacy was evaluated on days 4, 8, 15, and 29 after initiation of therapy and again 2 weeks after the end of treatment (day 43). Primary efficacy parameters included the physician's gross assessment of response to therapy, change from baseline in four individual sign and symptom scores (erythema, skin thickening, scaling, and pruritus), change from baseline in the total signs/symptoms score, and the patient's subjective evaluation. Gross assessment of the response of target lesions to treatment was based on a 4.0-point scale of severity of signs and symptoms that progressed in 0.5-point increments from 0.0 (absent) to 1.0 (mild), 2.0 (moderate), and 3.0 (severe). Patients' subjective assessments were based on a rating scale of excellent, good, fair, poor, or worse. Safety assessments were made on days 15, 29, and, if necessary, 43. Safety evaluations included adverse events, subnormal serum cortisol concentrations (morning serum cortisol measurement of <5 μg/100 mL or a ≥50% decrease from baseline), and laboratory evaluations.[18]

At least 80% of patients in each treatment group completed the 4-week treatment phase; however, significantly more patients in the clobetasol emollient group completed the 2-week posttreatment period (73% vs 41%; $P = 0.005$). Clobetasol emollient produced significantly greater improvement than did vehicle in the scores for total signs/symptoms, scaling by day 4, erythema and skin thickening by day 8, and pruritus by day 15 ($P \leq 0.006$). Mean reductions in all severity scores were significantly greater with clobetasol emollient than with vehicle throughout the rest of the treatment period; however, the mean change in pruritus score from baseline to day 29 was approximately the same as on day 15 in both

treatment groups. Two weeks after the end of treatment (day 43), the mean change in the scores for total signs/symptoms, erythema, scaling, and skin thickening remained the same as on day 29.

Physician's gross assessment and patients' self-assessment ratings for clobetasol emollient were superior to vehicle ($P < 0.02$ and $P \leq 0.05$, respectively). As the study progressed, the degree of improvement increased. Good, excellent, or cleared responses were more frequently reported in the clobetasol emollient group at day 29 than at day 15 in both the physician's gross assessment ratings (69% vs 48%) and patients' self-assessment ratings (85% vs 71%). These ratings were sustained during the posttreatment period (69% and 72%, respectively).

Drug-related adverse events were reported by five patients (11%) in each treatment group; all were considered mild to moderate. Five patients (11%) receiving clobetasol emollient and four (9%) receiving vehicle had burning or stinging that resolved on discontinuation of treatment. No differences were observed between the clobetasol emollient group and the vehicle group in the incidence of subnormal serum cortisol concentrations (one and zero patients, respectively). Two patients (5%) treated with clobetasol emollient and three patients (7%) receiving vehicle experienced a ≥50% decrease in serum cortisol concentrations from baseline during the study ($P = 0.664$); all other laboratory values remained within normal limits. One patient from each group withdrew because of a drug-related adverse event. One patient from the clobetasol emollient group (2%) and six from the vehicle group (13%) withdrew because of treatment failure. No patients from the clobetasol emollient group and 3 (7%) from the vehicle group failed to return; 4 patients from the clobetasol emollient group (9%) and 5 from the vehicle group (11%) withdrew for other reasons.

This study indicated that clobetasol propionate 0.05% emollient cream produces significantly greater improvement in patients with moderate-to-severe plaque-type psoriasis than does vehicle alone when administered twice daily for 4 weeks. Steady progression of improvement in signs and symptoms was confirmed by all investigator and patient ratings. This suggests that patients with severe plaque-type psoriasis who require >2 weeks of treatment may show improvement with an additional 2 weeks of treatment, and clobetasol emollient may be an appropriate alternative to other formulations in such cases. Furthermore, data from day 43 suggest that sudden cessation of treatment can be accomplished without acute worsening or return of signs and symptoms of psoriasis.[21]

CLOBETASOL EMOLLIENT CREAM IN THE TREATMENT OF PATIENTS WITH ATOPIC DERMATITIS

Clobetasol emollient cream was also evaluated in a double-masked, parallel-group, multicenter trial of 81 patients with moderate-to-severe atopic dermatitis, as reported by Maloney et al.[16] Eligible patients were nonhospitalized and ≥12 years old. They were randomized to receive twice-daily treatment with either emollient cream (n = 41) or vehicle (n = 40) for 4 consecutive weeks. A total of 37 patients using emollient cream and 24 patients using vehicle completed the study; 10 patients in the vehicle group dropped out of the study because of treatment failure. Patients who improved sufficiently

to discontinue therapy after 2 weeks underwent a 2-week nontreatment period, after which they were evaluated for recurrence of disease in the treated areas. The results showed that clobetasol propionate 0.05% emollient cream was safe and effective in patients with moderate-to-severe atopic dermatitis.

Patients received instruction in how to apply the study medication, and the first application was made in the presence of the investigator or a qualified assistant. Patients applied a fingertip unit, approximately 0.50 g in males and 0.43 g in females (enough to cover approximately 2% of the body surface area). Efficacy was evaluated at 3, 7, 14, and 28 days after initiation of therapy and again 2 weeks after the end of treatment (day 43). Primary efficacy parameters included the physician's gross assessment of improvement in the target lesion and individual and total severity scores for signs and symptoms (ie, erythema, pruritus, induration/papulation, lichenification, erosion/oozing/crusting, and scaling/dryness) involving the target lesion. Severity scores were based on a 4-point scale that progressed in 0.5-point increments from 0.0 (absent) to 1.0 (mild), 2.0 (moderate), and 3.0 (severe). Each patient's self-assessment of response to treatment was also documented at each follow-up visit. Safety assessments were made on days 15, 29, and, if necessary, 43. Safety evaluations included adverse events, the occurrence of subnormal serum cortisol concentrations (<5 μg/dL or a >50% decrease from baseline), and other laboratory abnormalities.

Although the majority of patients in both treatment groups completed the 4-week treatment phase of the study, significantly more patients in the clobetasol propionate group completed the 2-week posttreatment phase of the study (37 [90%] vs 24 [60%]; $P = 0.001$).[16,18] None of the patients in the clobetasol propionate group withdrew because of treatment failure, whereas 10 patients (25%) in the vehicle group withdrew from the study for this reason. No patients from either group withdrew because of a drug-related adverse event; no patients in the clobetasol propionate group and two patients in the vehicle group (5%) withdrew because of other adverse events. One patient in the clobetasol propionate group (2%) and 2 patients in the vehicle group (5%) failed to return; 3 patients in the clobetasol propionate group (7%) and 2 patients in the vehicle group (5%) withdrew for other reasons.[18]

Clobetasol emollient produced significantly ($P \leq 0.006$) greater improvement than did vehicle in scores for total signs/symptoms beginning at day 4 and continuing through the rest of the 4-week treatment phase and the posttreatment phase; score reduction increased progressively over time. Clobetasol emollient produced significantly ($P \leq 0.006$) greater improvement in target lesions than did vehicle by day 4 for some signs and symptoms (erythema, pruritus, induration/papulation, and scaling/dryness) and similar improvement by day 8 in other signs and symptoms (lichenification and erosion/oozing/crusting). All individual and total severity scores remained significantly lower in the clobetasol emollient group than in the vehicle group throughout the rest of the treatment period and during the 2 weeks posttreatment, except at day 43 for erosion/oozing/crusting.

Clobetasol emollient was superior to vehicle on physician's gross assessment, with more clobetasol emollient–treated

patients than vehicle-treated patients assessed as good, excellent, or cleared at both day 29 (82% vs 29%) and day 43 (78% vs 33%). Patients treated with clobetasol emollient reported significantly greater target lesion response to therapy than did patients treated with vehicle throughout the study period, beginning at day 4 and continuing through the post-treatment phase ($P \leq 0.002$). Significantly more patients in the clobetasol emollient group than in the vehicle group reported their response to be good or excellent at day 29 (84% vs 29%) and at day 43 (78% vs 42%).

Drug-related adverse events were reported in one patient in the clobetasol emollient group (pruritus, burning/stinging) and in two patients in the vehicle group (skin atrophy in one patient and pruritus in the other); none of these events were considered to be serious. Three patients (8%) in the clobetasol emollient group developed subnormal morning serum cortisol concentrations (<5 μg/dL) during the course of the study, compared with none in the vehicle group ($P = 0.240$). However, two of these patients had used 240 g of study drug during the 4-week treatment period instead of the 200 g specified by the protocol, as well as having had low-normal morning serum cortisol concentrations at baseline (5 and 7 μg/dL). Morning serum cortisol concentrations returned to normal by day 29 in two of these patients (despite continuation of treatment) and by day 43 in the third patient. The decreases in morning cortisol concentration were small and were not considered clinically significant. All other laboratory values remained within normal limits.

The results of this study indicate that clobetasol emollient 0.05%, applied twice daily for 4 weeks, is effective in the treatment of atopic dermatitis and has continuing efficacy for 2 weeks after discontinuation of treatment. Steady progression of improvement in signs and symptoms was confirmed by all investigator and patient ratings. This suggests that patients with atopic dermatitis who require ≥2 weeks of treatment may show improvement with an additional 2 weeks of treatment and may continue to progress after treatment is discontinued. Data from day 43 suggest that stopping clobetasol emollient therapy after 4 weeks of treatment does not result in an immediate return of signs and symptoms of disease.[16,18]

TOLERABILITY AND SAFETY

In a meta-analysis of controlled clinical trials that included patients with psoriasis or eczema and healthy volunteers treated or tested with the emollient formulation of clobetasol propionate,[18] adverse events judged to be possibly or probably related to clobetasol emollient treatment occurred in only 1.1% of study subjects.

With its demonstrated safety profile, this agent is indicated for 4 weeks' use in patients with severe plaque-type psoriasis when ≤10% of total body surface area is being treated.[18] The controlled clinical trial in patients with atopic dermatitis suggests that 4 weeks' use of this formulation is well tolerated in these patients as well. Total dosage of clobetasol propionate emollient cream should not exceed 50 g/wk because of the potential for HPA axis suppression. Clobetasol propionate emollient cream should not be used on the face, groin, or axillae or with occlusive dressings, and it is not recommended for treating children <16 years of age with plaque-type psoriasis or <12 years of age with other indications.

CONCLUSIONS

High-potency topical corticosteroids continue to offer a high degree of safety and efficacy in the topical treatment of patients with inflammatory and pruritic manifestations of moderate-to-severe corticosteroid-responsive dermatoses. In recent years, an improved understanding of the skin's natural remoisturization process has increased awareness of the potential benefits of emollient use in the management of dry skin conditions. A number of studies have provided evidence that emollients, used alone and in combination with topical corticosteroids, can have a beneficial effect in patients with dermatologic conditions characterized by dry skin, scaling, and plaque-type lesions.[13,19,21]

Clobetasol propionate is a group I steroid with demonstrated clinical value. In its emollient formulation, clobetasol propionate may help soothe dry skin associated with various dermatologic conditions and contribute to improved clinical results. Recent studies in the use of clobetasol emollient suggest that it is well tolerated and efficacious in courses of up to 4 weeks for the treatment of patients with plaque-type psoriasis or atopic dermatitis. Improvements in signs and symptoms may continue for 2 weeks after discontinuation of treatment.

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