Optimizing the Use of Topical Agents in Psoriasis

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Abstract

The vast majority of patients with psoriasis have localized disease that is manageable by topical therapy alone, and patients with more severe disease still require topical treatment for plaques that persist despite effective systemic treatment or phototherapy. Nevertheless, little attention today is paid to topical therapy, including new topical treatments. This article briefly addresses key issues that can adversely affect the use of and compliance with currently available topical treatments, as well as new and emerging topical agents for psoriasis.

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Keywords

Corticosteroids; JAK; Janus kinase inhibitors; phosphodiesterase-4 inhibitors; pimecrolimus; psoriasis treatment; skin atrophy; tacrolimus; topical; vitamin D

Most patients with psoriasis have localized cutaneous lesions. The majority—an estimated 70% to 80%—can be adequately treated with topical agents,[1] yet some effective topical treatments appear to be underused or to be prescribed in a way that is less than optimal. For example, in a population-based study of more than 27,000 patients with psoriasis, Stern and colleagues[2] determined that 83% of patients have localized plaques, covering 2% or less of body surface area (BSA). Nevertheless, these patients reported experiencing a substantial burden from their disease and consider their treatment to be less than satisfactory.

Topical Corticosteroid Therapy

Three commonly encountered issues that can adversely affect topical corticosteroid therapy for psoriasis are insufficient amounts of medication, concerns about skin atrophy, and allergic reactions. These issues are readily addressed in most cases.

To make compliance with a prescribed topical regimen possible, patients need to have available a sufficient amount of medication for the designated affected areas and duration of treatment. Consider that 0.55 g of medication should be provided for twice-daily application for each 1% of BSA. The **Table** below shows examples of the amount of medication required for 1 month of twice-daily applications according to BSA involvement.[3] For example, a 60-g tube of medication is more than sufficient for a patient with 3% BSA involvement (such as the soles of both feet), but a patient with full-scalp involvement—about 6% BSA involvement—will need almost 100 g for 1 month of treatment.

Concern over corticosteroid-related skin atrophy is a frequently discussed obstacle to use of this effective class of agents. Despite the perception by some that this is a widespread problem, the reported incidence of skin atrophy with some of the most effective topical treatments actually is quite low. As examples, no cases of skin atrophy were reported in the pivotal studies of clobetasol propionate 0.05% spray.[4] With the use of clobetasol propionate foam, 2% of patients with moderate to severe atopic dermatitis in the pivotal trials showed skin atrophy after 2 weeks of use vs 1% of patients who used vehicle only.[5] Similarly, no cases of atrophy have been reported for

TABLE Amount of Topical Medication Needed for 1 Month of Twice-Daily Applications

Area	% BSA	Grams Needed per Month
Scalp	6	99
Both elbows	2	33
Both knees	2	33
Both palms	2	33
Both soles	3	49.5
Face and neck	5	82.5
Trunk (anterior)	16	264
Trunk (posterior)	16	264
Leg, including foot	16	264
External genitalia	1	16.5
Buttocks	8	132

BSA=body surface area.
Source: Adapted from Menter et al.[3]

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fluocinonide 0.1% cream.[6] In a study of halobetasol propionate 0.05% cream and ointment in patients with atopic dermatitis or psoriasis, no cases were reported after 2 weeks of use; only one case of "mild" atrophy was reported in a pediatric patient with the use of halobetasol propionate 0.05% ointment.[7] Furthermore, according to Josse and colleagues,[8] when epidermal atrophy does occur with a topical corticosteroid, it is reversible on discontinuation of the medication.

Prevention of atrophy with corticosteroid use was the focus of several studies. In one, Lavker and colleagues[9] studied skin thickness with the use of ammonium lactate alone, clobetasol propionate alone, and the simultaneous use of both agents in a group of healthy patients. These investigators found that ammonium lactate use alone resulted in an average increase in epidermal thickness of 19%, use of clobetasol propionate alone decreased epidermal thickness by an average of 51%, and simultaneous use of both agents resulted in a net reduction in atrophy of 35%. In a study involving combined use of tazarotene and diflorasone diacetate 0.05% ointment, Kaidbey et al[10] showed that tazarotene alone increased epidermal thickness by 62%, vehicle alone increased thickness by 20%, and the corticosteroid decreased epidermal thickness by 43%. When these two agents were used in combination, atrophy was reduced by 37%.

Calcipotriol also tends to thicken the skin when used as monotherapy. In a study by Lévy and colleagues,[11] combination therapy was not used, but the investigators found that calcipotriol use tended to thicken the skin, whereas the corticosteroid caused thinning. Therefore, theoretically, it is possible that calcipotriol also may help minimize epidermal atrophy in corticosteroid users.

Duration of Topical Corticosteroid Therapy

Some studies examined the potential utility of topical corticosteroids for longer-term maintenance of remission. One such study involved betamethasone dipropionate ointment, with twice-daily applications for 2 to 3 weeks, followed by weekend-only with betamethasone dipropionate or vehicle.[12] The investigators found that 38 of 59 patients (64%) had an 85% improvement using the active medication for 2 to 3 weeks; 74% of this group maintained this level of improvement with weekend-only treatment, compared to 21% of patients who used vehicle alone on the weekends.

A second study involved the use of clobetasol propionate twice daily for 2 weeks.[13] Treatment led to clearance of psoriasis in 62% of patients. These patients were then switched to maintenance therapy with twice-weekly applications; 75% had maintained remission at 4 months.

Hanifin and colleagues[14] studied maintenance treatment with a corticosteroid in children and adults with atopic dermatitis. In this study, patients used fluticasone propionate cream plus emollients twice daily for 4 weeks, followed by tapering to twice-weekly applications of the active drug or vehicle-only, plus emollients, or emollients alone. Patients who were in the active-treatment group for twice-weekly applications were 7 to 8 times more likely to maintain remission than were those using emollient only or emollient plus vehicle.

These studies suggest that having patients continue to use a topical corticosteroid that has been effective for them, applied to the areas where they tend to flare, will result in longer periods of disease clearance.

Topical Corticosteroid Allergy

Allergy to topical corticosteroids is estimated in 0.2% to 5% of patients with dermatitis of any etiology.[15,16] In susceptible patients, a reaction can occur either on first exposure or after use over time. Corticosteroid allergy should be suspected in any patient who uses a topical agent and has no improvement at all, if the disease flares with use of the medication, or if initial improvement is seen followed by a flare when the treatment is interrupted.

An estimated 85% of patients with a corticosteroid allergy are likely to be sensitive to more than one type of agent. For example, an individual who has an allergic reaction to an agent in class B corticosteroids is more likely to be allergic to other agents in the same or other classes. In addition, cross-reactivity can be seen with class A and group D2 drugs. Class C drugs (desoximetasone, a potent agent, and clocortolone pivalate, which is in the midpotent classification) are least likely to cause allergic reactions.[17]

Allergy to an ingredient in the vehicle also should be considered. Propylene glycol allergy occurs in about 2.9% of patients. Other potential allergens commonly used in vehicles include sorbitan sesquioleate (up to 10%), dialkyl thiourea (1%), parabens (1.2%), and lanolin (1.8%).[18]

Topical Nonsteroidal Therapy

Vitamin D is essential for the normal healthy structure and function of skin. In patients with psoriasis, topical vitamin D has been shown to inhibit keratinocyte proliferation, induce keratinocyte differentiation, and reduce inflammation. Its use is associated with minimal side effects.[19,20] In one small open-label study, punch biopsies of patients treated with calcitriol twice daily for 4 weeks showed an increase over baseline in filaggrin—a key marker of differentiation.[21] Vitamin D formulations seem to be especially helpful for treating psoriatic plaques in sensitive areas, including the face, under the breasts, the axillae, and the groin—anatomic sites in which a potent corticosteroid should be avoided and where vitamin D is likely to be effective as monotherapy because of greater penetration achieved in the thinner skin in these sensitive areas. Topical immunomodulators—pimecrolimus and tacrolimus—represent another option for monotherapy for the face or intertriginous areas. For plaques on other skin sites, vitamin D formulations and topical immunomodulators are not optimal as monotherapy. However, as a landmark study by Lebwohl and colleagues demonstrated,[22] combination therapy with vitamin D and potent corticosteroids can be highly effective.

Tazarotene is often not considered for treating psoriasis, but both the 0.1% and the 0.5% cream and gel are approved by the US Food and Drug Administration for this indication. Again, combination therapy with a potent or midpotency corticosteroid seems to yield the greatest efficacy.[23]

Finally, among the noncorticosteroid options, tar may be appropriate in selected patients. Despite its demonstrated efficacy and safety, the aesthetic objections to tar relegated this agent to near the bottom of the list of options for psoriasis therapy once other effective medications—especially topical corticosteroids—became available. However, with the introduction of formulations of tar in newer vehicles (a 2.3% solution and a 2% foam), the use of tar is again an acceptable option for treating psoriasis in selected patients.

Emerging Topical Treatments

Some promising new treatments for psoriasis currently are being investigated, including Janus kinase (JAK) pathway inhibitors and phosphodiesterase (PDE) inhibitors.

JAK is one of many intracellular pathways found to be present on cell membrane surfaces. Cytokines bind to JAK pairs (JAK 1, 2, 3 and TYK2). One agent, tofacitinib, preferentially inhibits JAK 3 and/or JAK 1, and an ointment combining this drug and a penetration enhancer appears to be helpful in patients with mild to moderate plaque psoriasis. Tofacitinib and other inhibitors of JAK currently are being investigated.

A PDE type 4 inhibitor, a boron-based molecule shown to have anti-inflammatory properties, has been studied for mild to moderate plaque psoriasis and also shows promise. Studies are under way using an ointment formulation.

Conclusion

Topical therapy has an important role in plaque psoriasis in appropriately selected patients. Clinicians should be vigilant for the development of cutaneous atrophy; however, if it does develop, it is easily reversible with cessation of therapy. Vitamin D has an important role in psoriasis; new formulations of tar and tazarotene cream/gel should be considered in the appropriate clinical circumstances. New molecules for the topical treatment of psoriasis currently are in development and hold promise as potentially valuable additions to the topical treatment armamentarium.

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