

Topical Medications: A Focus on Antifungals and Topical Steroids

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Because skin disease is accessible, it can be treated with locally applied medication, which offers great advantages—exposure to a drug is limited to the affected skin and systemic effects of potentially toxic drugs are minimized. Ointments, creams, antifungals, and antibiotics all have their place in treating various skin diseases. Topical steroids, the largest group of topical medications, are effective but present the potential for side effects. This article discusses current and new topical medications that can be used to treat a range of skin diseases.

VEHICLES IN DERMATOLOGIC THERAPY

The old adage “if it’s wet, dry it; and if it’s dry, wet it” speaks to the importance of vehicles in dermatologic therapy. In the past, the vehicle *was* the medicine. Now that we have dermatologic drugs that work, keeping the skin dry or wet is a peripheral consideration. Rather, the primary considerations in prescribing medication are delivery of the drug to the skin and protection of barrier function. Another important consideration is the cosmetic acceptability of the preparation. If the patient won’t use it, even the best drug won’t do any good.

Ointments are best at delivering a drug to the skin and protecting barrier function, eg, petrolatum. Creams, which are oil in water emulsions, are less greasy (eg, cold cream) and more acceptable to patients but are generally less effective than ointments. In addition, poorly designed creams (of which there are many) are often irritating and may actually worsen some skin diseases. Lotions are diluted creams. Solutions are typically alcoholic

KEY POINT

Delivery of the drug to the skin and protection of barrier function are the primary considerations in prescribing dermatologic medication. Cosmetic acceptability is also important—if the patient won’t use it, even the best drug won’t do any good.

liquids and are especially useful for treating the scalp because they don’t coat the hair.

General wisdom says that patients prefer creams; however, this is true only if the patient has a mild or short-duration disease. The experienced patient with a chronic skin disease will often insist on the ointment form of a medication knowing that it is more effective. Greasy medications should not be applied in a thick layer. Usually it is sufficient to lightly coat the affected skin with an amount that

will be absorbed in a few minutes. Excess ointment that can be wiped away should be avoided.

TOPICAL ANTIFUNGALS

Many topical antifungals are now available but not all are equally effective. Nystatin and miconazole are particularly effective for treating the *Candida* species, and they are fine for intertrigo but not effective for ringworm. Most dermatologists agree that clotrimazole is relatively inactive compared with more recently introduced compounds such as terbinafine, ciclopirox olamine, and butenafine.

Topical therapy is appropriate for superficial fungal infections, including tinea of the trunk and extremities, candidal intertrigo, paronychia, and tinea versicolor (also known as pityriasis versicolor). However, when fungus infection involves hair follicles, as in tinea capitis or Majocchi's granuloma, topical medication is usually ineffective and oral medication is the best initial treatment. At least 2 weeks are required for the effective treatment of any dermatophytic infection using a cream; howev-

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er, tinea versicolor responds within days. Athlete's foot, jock itch, and intertrigo are dermatophytic infections caused in part by excess moisture due to anatomic occlusion of the site; effective therapy always includes an effort to correct the overhydration. Treating athlete's foot is more complicated because in addition to overhydration, which promotes the initial fungal infection, there is often a secondary bacterial colonization or infection that produces dramatic maceration and ulceration. Patients whose interdigital maceration does not resolve with topical antifungal therapy often benefit from having a bacterial culture taken, followed by treatment with an appropriate oral antibiotic.

Topical antifungals are also indicated in seborrheic dermatitis. Although the cause of seborrheic dermatitis is unknown, it is clear that topical

ketoconazole and ciclopirox olamine will control scaling and inflammation. This approach is much safer than prescribing topical glucocorticoids, which have a very low margin of safety when used on the face.

TOPICAL ANTIBACTERIALS

Only a few topical antibiotics are available for treating skin diseases. For acne, there are benzoyl peroxide, erythromycin, and clindamycin. For local infections, such as impetigo, there are mupirocin, polymyxin, bacitracin, and neomycin; however, contact allergy is a particular problem with preparations containing polymyxin, bacitracin, and neomycin, and their use should be used with discretion or avoided.

Topical antibacterial therapy is appropriate in superficial impetigo, folliculitis, and prophylaxis of wound infection. At least 1 week of treatment is required.

TOPICAL STEROIDS

Steroids, by far, comprise the largest group of topical medications. When introduced in the 1960s, topical steroids changed our approach to treating inflammatory skin diseases; however, since then we have become aware of certain problems they cause (1) (Table). The greatest adverse effect of topical steroid use is skin atrophy. Atrophy occurs most quickly with the stronger steroids but also can be caused by over-the-counter hydrocortisone if the patient is diligent in using it. Thin skin is more susceptible to atrophy; the face and groin thin most quickly and the palms least quickly. Moreover, preexisting atrophy from systemic steroid use or sun damage will greatly accelerate the development of atrophy due to topical steroid use. The extensor forearm of most fair-skinned 50-year-olds will not tolerate prolonged steroid use without becoming fragile. Small children are at greatest risk.

KEY POINT

The greatest adverse effect of topical steroid usage is skin atrophy.

TABLE.

ADVERSE EFFECTS OF
TOPICAL CORTICOSTEROIDS

- Atrophy
 - Bruising
 - Fragile skin
 - Easy irritation
 - Striae
- Worsening of previously controlled disease despite therapy
- Masking of signs of infection, especially with dermatophytes
- Masking an underlying disease, eg, lymphoma or lupus erythematosus
- Ophthalmic
 - Cataracts
 - Glaucoma

Signs of atrophy include easy bruising, a shiny appearance, striae, and a worsening of the disease despite the use of medication. Disease exacerbation can be difficult to appreciate as a sign of steroid atrophy since we are predisposed to medications being effective. In atopic dermatitis, for example, it is common to see increasingly stronger steroids prescribed in response to atrophy-induced disease exacerbations.

Clinically significant suppression of the hypothalamic-pituitary axis is rarely seen but can be measured following the long-term use of potent steroids. Topical steroids can also potentiate or cause cataract formation or glaucoma when used around the eyes for prolonged periods.

A second caveat regarding the use of topical steroids involves their ability to suppress many diseases for which their use was not intended. Dermatophytic infections, systemic lupus erythematosus, and cutaneous T-cell lymphoma will all respond to mid- to high-potency steroids.

It is essential to reach a diagnosis before starting skin treatment with a steroid. If a therapeutic trial of steroid therapy is implemented for a disease that eludes diagnosis, then a clear and relatively brief time limit should be set for the treatment. If the disease recurs, potentially serious disorders must be ruled out before steroid treatment can be resumed. Combination products, that is, products in which a steroid and an antifungal are combined,

do not offer significant benefits—either a disease is infectious, in which case the steroid is of no use, or it is inflammatory and the antifungal is wasted. A correct diagnosis should always precede treatment.

Steroid potency is modulated by the substitution of the steroid nucleus and by modifications of the vehicle. Topical steroids are ranked in potency according to their ability to cause vasoconstriction under defined conditions (2). Although this test does not measure efficacy in disease, it is a very sensitive measure of the relative potency of topical steroids.

Three Principles of Topical Steroid Therapy

Drug company claims aside, the first principle of topical steroid use is that steroid potency is directly proportional to the potential for side effects. It does not matter by what means (eg, halogenation, fatty acid substitution, or vehicle manipulation) a steroid product is made potent—potency determines local side effects.

KEY POINT

The 3 principles of topical steroid therapy are: steroid potency is directly proportional to the potential for side effects; generic topical steroid preparations do not duplicate the vehicle of the brand-name product; and when a stronger steroid is needed, switch to another class of steroid potency rather than increase the percentage of the same drug.

The second principle is that generic topical steroid preparations do not duplicate the vehicle of the brand-name product (3) and may not be of equal efficacy. It is not uncommon to see a patient who is well controlled with a brand-name topical steroid suddenly experience a flare of disease after switching to a generic substitute or a different generic preparation.

The third principle is that when a skin disease is unresponsive and a stronger steroid is needed, switch to another class of steroid potency rather than increase the percentage of the same drug being

used; in other words, 0.1% triamcinolone is not significantly more potent than 0.025% triamcinolone.

Selection and Treatment

Selection of a topical steroid is based on balancing the resistance of the skin disease with the potential for skin atrophy. Lichen planus, discoid lupus erythematosus, and lichen simplex chronicus usually require potent topical steroids partially because of the depth of the inflammatory process in the skin. Deeper diseases, such as cutaneous sarcoidosis, are generally unresponsive to topical therapy. In such diseases the surface of the skin will atrophy before the deeper inciting inflammation responds to treatment. Superficial diseases, such as psoriasis and atopic dermatitis, often can be controlled by mid-potency drugs. Self-limiting diseases such as poison ivy can be treated briefly with potent steroids to get quick relief. In general, children can be effectively treated with low-potency steroids.

Chronic hand dermatitis is a particularly difficult problem. Often there is a work-related component and long-lasting relief is not achieved quickly. Two diseases account for most chronic hand problems—psoriasis and atopic dermatitis. Both are exacerbated by irritation and trauma and both respond to steroids. The difficulty in treatment centers on the need to use strong steroids to get palmar skin to respond and their propensity to cause skin atrophy, which then increases skin irritability and causes the disease to recur. As more steroids are needed to control flares, a vicious circle develops. The key to avoiding this common situation is to use potent steroids for a brief period of time and to focus on the removal of exacerbating factors.

TOPICAL IMMUNOSUPPRESSIVES

A new class of topical medication has now become available—nonsteroidal topical immunosuppressives. Currently only tacrolimus, a cyclosporin-like inhibitor of T-cell activation, is available in topical form. Topical tacrolimus, which is indicated for atopic dermatitis, is a real boon for many patients. The drug is as potent as a strong topical steroid but free of significant side effects, including (and especially) skin atrophy, and it is safe for periorcular

application. Atopic patients who were previously poorly controlled on systemic and topical steroids have shown dramatic and lasting improvement when treated with tacrolimus.

TOPICAL ANTIVIRALS

Most dermatologists believe that topical antiherpes medications are relatively ineffective in treating genital or orofacial herpes. Topical imiquimod is an interferon inducer that after prolonged application will induce regression of genital warts. It is most effective on warts that are in occluded areas. Irritation may result, but it is generally less than that caused by destructive wart therapy.

OTHER TOPICAL MEDICATIONS

5-fluorouracil is available in topical form for the treatment of premalignant actinic keratoses. The target cells preferentially take up the drug and are poisoned. Two to 3 weeks of treatment are necessary and significant irritation can be expected. However, a newer microsphere-delivered gel avoids some of this irritation.

Calcipotriene, a vitamin D derivative, is helpful in treating psoriasis. Its strength is its freedom from the atrophogenic effects of steroids; however, in the experience of most dermatologists, it is also much less effective than mid-potency steroids. The drug is typically used as maintenance therapy along with occasional topical steroid use.

SUMMARY

Topical medications minimize systemic effects but may enhance local side effects. Topical steroids in particular can cause local problems with prolonged use. The new immunosuppressives, however, show promise in delivering the potency of a steroid but without the side effects.

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Dialogue Box

ADVISORY BOARD

Are some types of steroid formulations safer than others with respect to skin atrophy?

WEBSTER

The truth is that steroid potency and atrophogenicity are inseparably linked. This is true even with the so-called “soft steroids” that are metabolized into prednisolone. Because they’re metabolized in the skin, soft steroids cause less hypothalamic-pituitary axis suppression since there is a less potent steroid metabolite circulating. Even from the skin’s point of view, the soft steroids are atrophogenic in proportion to their potency. Although some drug companies would have you believe that certain potent steroid formulations are safer because they are not fluorinated, the bottom line is that the risk for atrophy is a function of potency regardless of whether or not the steroid is fluorinated.

ADVISORY BOARD

In the past, what was the rationale for the common practice of occluding an area being treated with a topical steroid with cellophane? Is this technique used anymore?

WEBSTER

The idea was simply that occlusion facilitated better penetration, which translated into a greater effect. In the past when you were using steroids of limited potency, occlusion was really important. This was particularly the case in patients with psoriasis where occluding with an agent such as Lidex[®] was necessary to enhance its potency and achieve the desired effect. Nowadays, there are other ways to do it. You can add a little salicylic acid to the preparation, which will enhance penetration of the steroid preparation tremendously. Most physicians today, especially the younger ones who haven’t had to occlude to increase steroid potency, just prescribe something very

strong such as Temovate[®], Diprolene[®], or Ultravate[®] and so they hardly ever need to occlude.

ADVISORY BOARD

How large a sample do you have to send to optimally culture a dermatophyte from a suspected tinea lesion?

WEBSTER

Dermatophytes can be incredibly fastidious organisms to grow. They have to be happy and you have to have a ton of scale in there, and even then they don’t necessarily grow well. Thus, a negative culture doesn’t mean that a dermatophyte is not present. It is for this reason that I have found the potassium hydroxide (KOH) skin prep to be of immense clinical value. All you need is a little bit of scale on a slide, a 10% KOH solution, a cover slip and microscope, and a trained eye.

ADVISORY BOARD

What if the KOH prep is negative?

WEBSTER

If you’re trying to sort out whether you’re dealing with an inflammatory disease or a dermatophyte infection, another option would be a shave biopsy. If the question is what specific inflammatory disease are you dealing with, you may not get an adequate amount of tissue with a shave, and a punch biopsy would be a better way to go.

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In trying to rule in or out a dermatophytic or fungal skin infection, some clinicians simply give the patient a diagnostic and therapeutic trial of a topical steroid, reasoning that if the rash gets worse, then they’re dealing with a tinea infection, and if it gets better, then a fungus is not responsible. What are your thoughts regarding such a method?



Dialogue Box

WEBSTER

Such an approach absolutely doesn't work. In dermatology circles we have this thing that we snicker about called "tinea incognito." This is basically tinea that's been treated with a steroid for so long that it's clinically quiet but progressive. In this scenario, you can see the giant arcs of ringworm across a patient's body that grew from a tiny point of origin as a result of having a steroid put on them. It looks exactly like the tinea you see in people who have a specific anergy to a dermatophyte. It's barely inflammatory but incredibly widespread.

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Does topical ketoconazole or ciclopirox cure seborrheic dermatitis? Have dermatophytes

been implicated as the causative agent in its pathogenesis?

WEBSTER

No, but those agents do reduce the inflammation. The normal flora yeast, *Pityrosporum orbiculare*, which lives in the pilosebaceous areas and is the same organism that causes tinea versicolor, has been implicated in the pathogenesis of seborrheic dermatitis primarily on the basis that antifungals work in this common disorder. The conundrum is apparent when you ask why does oral ketoconazole always cure tinea versicolor but rarely cures or treats seborrheic dermatitis? The answer has to be that with seborrheic dermatitis ketoconazole is not working as an antifungal but instead as an anti-inflammatory agent.