TOPICAL CORTICOSTEROIDS.WHICH DRUG AND WHEN?

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Topical Corticosteroids
Which Drug and When?

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Contents

65 Summary
66 1. General Recommendations
67 2. Specific Indications for Topical Corticosteroid Treatment
67 2.1 Topical Corticosteroids as the Treatment of Choice
67 2.1.1 Eczema
67 2.1.2 Lichen Planus
68 2.1.3 Lichen Simplex Chronicus (Circumscribed Chronic Dermatitis, Neurodermatitis)
68 2.1.4 Insect or Arthropod Bite Reactions
68 2.1.5 Burns and Sunburns
68 2.1.6 Keloids
68 2.2 Topical Corticosteroids as Useful Alternative and/or Adjuvant Treatment
68 2.2.1 Psoriasis
68 2.2.2 Seborrhoeic Dermatitis
68 2.2.3 Diaper Dermatitis ('Nappy Rash')
69 2.2.4 Miscellaneous Disorders
69 2.3 Skin Diseases in which Topical Corticosteroids have to be Confirmed as Useful
70 2.4 Topical Corticosteroids as Symptomatic Treatment
70 3. Combination Preparations
70 4. Conclusions

Summary

A number of factors have to be taken into account when dealing with the treatment of skin diseases with topical corticosteroids, including disease type and phase, potency of the drug, safety, site to be treated, age of the patient, and drug formulation.

Concerning the specific indications for topical corticosteroid treatment, we can distinguish skin diseases in which: (a) topical corticosteroids are the treatment of choice; (b) topical corticosteroids are useful as alternative and/or adjuvant treatment; (c) the proposed use of topical corticosteroids has to be confirmed as useful; and (d) topical corticosteroids can be used as a symptomatic treatment. Within these groups, the treatment schedule has to be adjusted according to the abovementioned general factors.

When dealing with the treatment of skin diseases with topical corticosteroids, several parameters have to be taken into account. Generally speaking, the careful evaluation of at least the most important factors affecting treatment – disease type, site and severity; potency, safety and formulation of the drug (table I) [Miller & Munro 1980; Polano 1984]; and patient age – is the necessary prerequisite for appropriate, safe, and successful therapy (August 1989; Giannotti 1988; Pierard et al. 1989; Takeda et al. 1988; Uppal et al. 1991).

1. General Recommendations

A short and simple list of general guidelines for the topical treatment of skin diseases with corticosteroids can be given (Giannotti 1988):

1. Short term or intermittent use of potent corticosteroids, to reduce the risk of local and systemic side effects and to prevent tachyphylaxis (du Vivier 1976; Hradil et al. 1978; Katz et al. 1987a,b; Lubach et al. 1989; Takeda et al. 1988; Van der Harst et al. 1982).

2. Avoidance of sudden discontinuation of treatment, to prevent rebound phenomena. Upon improvement, the use of a less potent preparation, or the alternate use of topical corticosteroids and emollient preparations, is recommended until a complete resolution of the clinical lesions is achieved (Cullen 1989; Harper 1988; Takeda et al. 1988; Thiers 1989; Turpeinen 1991).

3. Use of low potency corticosteroids to treat children, large areas of the body, and anatomic sites especially susceptible of steroid damage (e.g. on the face, flexures, or scrotum). The application of higher potency drugs must be limited to areas resistant to treatment with mild preparations, possibly alternated with the latter.

4. Choice of the vehicle depending on the type and site of lesion (oil in water lotions and creams for acute and weeping lesions; lotions, creams or gels preferable for hairy areas and flexures; and ointments or water in oil creams for dry and chronic lesions).

5. Performance of clinical and laboratory tests if the drug is used for long periods and/or on large areas of the body.

Several preparations of corticosteroids are also available for intralesional injection. Triamcinolone acetonide (or diacetate) or methylprednisolone, diluted in carbocaine 1% and distilled water, can be used in specific circumstances (Verbov 1976). As a general rule, the quantity of solution to be in-

Table I. Clinical potencies of topical corticosteroids (adapted from Miller & Munro 1980; Polano 1984)

Mild (class I)
Dexamethasone 0.01%
Hydrocortisone (alcohol or acetate) 0.1-1%
Methylprednisolone 0.25%
Moderately potent (class II)
Clobetasone butyrate 0.05%
Flumethasone pivalate 0.02%
Fluocinolone acetonide 0.01%
Fluocortin butylester 0.75%
Fluocortolone pivalate 0.2%
Fludroxycortide (flurandrenolone) 0.0125-0.025%
Hydrocortisone 1% with urea
Potent (class III)
Beclomethasone dipropionate 0.025%
Betamethasone benzoate 0.025%
Betamethasone dipropionate 0.05%
Betamethasone valerate 0.1%
Budesonide 0.025%
Desonide 0.05%
Desoximethasone 0.25%
Diflorasone diacetate 0.05%
Diflucortolone valerate 0.1%
Fluclorolone acetonide 0.025%
Fluocinolone acetonide 0.025%
Fluocinonide 0.05%
Fluocortolone pivalate 0.5%
Fluprednidene (fluprednylidene) acetate 0.1%
Fludroxycortide (flurandrenolone) 0.05%
Halcinonide 0.1%
Hydrocortisone butyrate 0.1%
Triamcinolone acetonide 0.1%
Very potent (class IV)
Beclomethasone dipropionate 0.5%
Clobetasol propionate 0.05%
Diflucortolone valerate 0.3%
Fluocinolone acetonide 0.2%
Ulobetasol (halobetasol) 0.05%
Mometasone furoate 0.1%
Prednicarbate

jected is scheduled according to the size and thickness of the lesion; it is absolutely useless, in fact, to inject more solution than that can be immediately adsorbed by the tissue.

2. Specific Indications for Topical Corticosteroid Treatment

In order to make clear the practical guidelines for the treatment of specific skin conditions with topical corticosteroids, we will consider 4 main groups of diseases: (a) those in which topical corticosteroids are the treatment of choice; (b) those in which topical corticosteroids are useful as alternative and/or adjuvant treatment; (c) those in which the proposed use of topical corticosteroids has to be confirmed as useful; and, (d) those in which topical corticosteroids can be used as symptomatic treatment (in addition to specific therapy).

2.1 Topical Corticosteroids as the Treatment of Choice

2.1.1 Eczema

Contact Dermatitis

In allergic contact dermatitis, moderately potent (class II) topical corticosteroids are usually sufficient to control the clinical evolution of the disease, along with the avoidance of the contact allergen. In selected cases of chronic lichenified lesions, a class III or IV topical corticosteroid may be required. In any case, it is wise to avoid a sudden discontinuation of the treatment (Ortonne 1988; Vilgioglia et al. 1990). The possibility that topical corticosteroids, especially hydrocortisone, induce allergic sensitisation must not be forgotten when dealing with chronic forms becoming resistant to topical treatment (Wilkinson et al. 1991).

In irritant contact dermatitis, the treatment with class I or II topical corticosteroids is generally effective (Ortonne 1988). Recent studies, however, raise doubts regarding the superiority of topical corticosteroids versus emollient creams and ointments in controlling the basic feature of skin irritation, i.e. dryness due to increased water loss (Van der Valk & Maibach 1989).

Atopic Dermatitis

The weakest topical corticosteroids are recommended in this condition, due to the simple consideration that this is a chronic disease and most patients are children. Class II to IV topical corticosteroids may be required for the treatment of acute exacerbations or severely lichenified lesions, accompanied by oral antihistamines and corticosteroids when necessary. In this case, rapid replacement with decreasingly potent topical corticosteroids, until complete discontinuation, is recommended (Harper 1988; Ortonne 1988; Thiers 1989; Vilgioglia et al. 1990). In any case, the removal of exacerbating agents and modifying behaviour to avoid situations that may cause irritation are of substantial help in the treatment of atopic dermatitis (Noren & Melin 1989). The continuous use of nonirritant detergents and emollient creams and ointments must be recommended, and is of primary importance in the correct management of the disease. In particular, a greasy vehicle and alternate use of topical corticosteroids with emollients in dry skin and chronic lesions is preferable.

Other Types of Eczema

In nummular eczema, the use of mild to moderate topical corticosteroids – gradually discontinued – is recommended. In stasis eczema, mild to moderate topical corticosteroids are indicated as well. The proper pharmacological and nonpharmacological treatment of vascular disturbances (i.e. venous insufficiency of the lower limbs) is however of primary importance in the prophylaxis of this type of disorder. Combination preparations of weak topical corticosteroids and urea are very effective in asteatotic eczema

2.1.2 Lichen Planus

In cases with localised lesions, topical corticosteroids may be sufficient. Potent or very potent topical corticosteroids, possibly under plastic occlusion, or in selected cases intralesional cortico-

steroids (triamcinolone acetonide 5 to 10 mg/ml), may be useful in the treatment of hypertrophic lesions or in lesions involving the nails, and may obviate the need for systemic steroids. In oral lesions, triamcinolone acetonide 0.1% in carmellose ('Orabase') may be very helpful.

2.1.3 Lichen Simplex Chronicus (Circumscribed Chronic Dermatitis, Neurodermatitis)

In this common disorder, short term courses of class III or IV topical corticosteroids, or intralesional triamcinolone acetonide 5 to 10 mg/ml in severely lichenified lesions, are generally highly effective.

2.1.4 Insect and Arthropod Bite Reactions

Moderately potent topical corticosteroids are generally effective in common insect bites, preferably in association with oral antihistamines and, in severe reactions, systemic corticosteroids. Due to possible microbial superinfections, particularly in bullous lesions, concomitant antibiotics may be required in selected cases. In persistent, isolated papulonodular reactions, intralesional triamcinolone acetonide 5 to 10 mg/ml may be very effective.

2.1.5 Burns and Sunburns

In first and second degree localised burns, as well as in mild to severe sunburns, class II topical corticosteroids are effective in relieving pain and reducing inflammation. In second degree lesions, the association with antibiotics is advisable, due to the frequent occurrence of microbial superinfections as a result of epidermal damage.

2.1.6 Keloids

Intralesional triamcinolone acetonide 10 to 40 mg/ml is the treatment of choice in keloids, and in hypertrophic scars which do not resolve spontaneously. Unsatisfactory results are often obtained when these lesions are treated in advanced stages.

2.2 Topical Corticosteroids as Useful Alternative and/or Adjuvant Treatment

2.2.1 Psoriasis

This is the most common dermatosis in which topical corticosteroids are one of the possible treatments, along with dithranol, photochemotherapy, oral retinoids, and more recently oral cyclosporin.

Topical corticosteroids are definitely useful in most patients with localised involvement. The weaker preparations are rarely effective; class III or IV topical corticosteroids, possibly under plastic occlusion or even occlusive dressings (David & Lowe 1989; Juhlin 1989), are generally very useful (Katz et al. 1987a, 1989; Trozac 1990; Watson et al. 1990). Continuous topical corticosteroid treatment should be avoided, in order to prevent rapid tachyphylaxis and local side effects; thus, intermittent use is recommended (Hradil et al. 1978; Katz et al. 1987b; Van der Harst et al. 1982), using a topical corticosteroid every other day, twice weekly, or on 2 consecutive days followed by a 3 day break.

Intralesional treatment with triamcinolone acetonide 5 to 10 mg/ml is indicated for isolated, chronic lesions.

2.2.2 Seborrhoeic Dermatitis

The use of topical corticosteroids should be limited to short, intermittent courses of class I or II preparations in patients with this condition, especially in extensive and acute lesions, to avoid dangerous local side effects on the face, the most frequently affected area. Local application of imidazole antifungals (e.g. econazole, clotrimazole, miconazole, bifemazole, isoconazole and ketoconazole) have a high therapeutic potential in seborrhoeic dermatitis (Katsambas et al. 1989), and the relevant aetiological role of the yeast *Pityrosporum ovale* may account for this clinical evidence. Therefore, a combined or alternate treatment should also be considered.

2.2.3 Diaper Dermatitis ('Nappy Rash')

The treatment of this disorder, very frequent in children, is principally based on the application of a 'barrier cream' (e.g. zinc oxide–containing prep-

arations) after every nappy change. In severe cases, weak topical corticosteroids are helpful; the addition of antifungal drugs or antibiotics is required when *Candida albicans* or bacterial infection coexists. The use of potent fluorinated topical corticosteroids is contraindicated (Harper 1988).

2.2.4 Miscellaneous Disorders

The treatment of *disidrosis (pompholyx)* is mainly based on the use of potassium permanganate soaks and moderately potent topical corticosteroids, possibly accompanied by oral corticosteroids and antihistamines in severe cases.

In *nodular prurigo*, short term courses of class III or IV topical corticosteroids, or intralesional triamcinolone acetonide 5 to 10 mg/ml, are generally highly effective.

Potent topical corticosteroids, under plastic occlusion, are effective in the treatment of *chronic discoid lupus erythematosus*, but the common involvement of the face definitely limits their long term use. In resistant cases, intralesional injections can be used, especially in mildly atrophic lesions (Callen 1990).

Granuloma annulare and *necrobiosis lipoidica*: topical treatment with corticosteroids, mainly triamcinolone acetonide 5 to 10 mg/ml injected intradermally, may be effective, but local side effects, such as severe dermal atrophy and/or sclerosis, have to be warranted.

Treatment with class II or III topical corticosteroids may definitely be helpful in *alopecia areata*, particularly in the early phases. Intralesional triamcinolone 5 mg/ml injections are indicated for the treatment of small areas.

Lymphocytic infiltration of the skin (Jessner-Kanof) responds well to class II topical corticosteroids, again with the limitation of short term use for lesions on the face.

The most widely known type of cutaneous lymphoma, *mycosis fungoides*, may also be satisfactorily controlled by class III topical corticosteroids in its early patch stage in patients with a limited number of lesions.

In *acne*, nonmicrobial inflamed cysts may be successfully treated with intralesional triamcinolone 2.5 mg/ml.

Topical corticosteroids can be useful in *aphthous stomatitis*, especially if applied in the early phases. Triamcinolone 0.1% in carmellose, possibly associated with oxyquinoline sulfate 0.1%, should be applied at least 4 times a day. The treatment has usually to be accompanied by an oral tetracycline, a topical anaesthetic [e.g. lidocaine (lignocaine) gel 2%], and systemic corticosteroids in severe cases.

Among bullous diseases, *familial benign pemphigus of Hailey-Hailey* can be satisfactorily treated with topical corticosteroids, alternated, or associated, with appropriate antimicrobial agents.

2.3 Skin Diseases in which Topical Corticosteroids have to be Confirmed as Useful

Bullous pemphigoid may be controlled in selected cases by potent topical corticosteroids (Westerhof 1989), thus allowing a useful saving of systemic steroid treatment. Moreover, topical corticosteroids may be useful as adjuvant treatment when single new lesions appear during the gradual dose reduction of oral corticosteroids.

The use of potent topical corticosteroids for the treatment of *cutaneous mastocytosis* has been proposed (Guzzo et al. 1991; Lavker et al. 1987), but the possibility of severe dermal atrophy has to be seriously taken into account. Even in *pyoderma gangrenosum*, combination treatment with potent topical corticosteroids and oral tetracyclines has been quite recently proposed in selected cases (Reynolds & Peachey 1990).

The treatment of *lichen sclerosus et atrophicus* with class IV topical corticosteroids is now proposed as definitely more effective in comparison with the classically used testosterone 2% ointments; a twice daily application seems to be the preferred schedule (Dalziel et al. 1989).

Finally, topical corticosteroids have been shown to promote the repigmentation in localised *vitiligo* (Liu et al. 1990).

2.4 Topical Corticosteroids as Symptomatic Treatment

Dermatophyte and yeast infections of the skin, when characterised by severe inflammation, heal faster and better with topical corticosteroids added to the specific treatment (mainly local imidazoles), without any compromise of long term efficacy. Indeed, *Candida* infections of the flexures may not clear at all with the use of a suitable antifungal preparation alone (August 1989). Patients must, however, be advised to limit the use of topical corticosteroids to the first days of treatment. The immediate efficacy of topical corticosteroids in reducing inflammation may generate the erroneous idea that this is the 'right treatment', and lead to inappropriately long term use. For this reason, it is sometimes wise to give short term systemic treatment with low dose corticosteroids instead of a topical combination treatment.

3. Combination Preparations

A relatively large number of preparations in which corticosteroids are combined with antimicrobial agents are currently available. This type of formulation is definitely more popular among general practitioners than among dermatologists, thus generating the suspicion that they are generally used when a precise diagnosis is lacking. This use, which is obviously questionable, should not however result in an indiscriminate lack of use of these preparations. Several dermatoses may be well suited to treatment with such a combination. In a clinical trial comparing the use of isoconazole 1% alone versus the same drug combined with diflucortolone 0.1% in dermatophyte and *Candida* infections, the latter preparation was found to be significantly more effective than the former, with regard not only to regression of signs and symptoms, but also to mycological cure rate. This clinical effect is presumably due to the greater bioavailability of the antifungal agent in the epidermis, due to the local vasoconstrictive activity of the corticosteroid, which allows a less rapid 'wash out' of the antifungal drug by the dermal microcirculation (reviewed in Hoppe 1988).

The literature contains conflicting reports regarding the effectiveness of corticosteroid-antibiotic combinations in secondary infected dermatoses, such as impetiginised atopic and contact dermatitis. Some authors failed to find a difference between corticosteroids used alone or in combination with antibiotics (mainly neomycin), while others found more clinical benefit by using combination preparations (reviewed in Giannotti 1988).

Combinations of topical corticosteroids with other substances are also available: urea, helpful in patients with xerotic skin for its moisturising effect; coal tar, in psoriasis, chronic eczema, and atopic dermatitis; and salicylic acid, indicated in cases with coexistent hyperkeratosis.

4. Conclusions

Topical corticosteroids are likely to remain a very effective, and indeed the only sensible, treatment of many skin disorders. Thus, an increasingly more suitable balance among efficacy, safety (local and systemic), and treatment compliance is the real goal of pharmacological research in the field of topical corticosteroids. High lipophilicity (with consequent quick penetration), and bioactivation in the skin (with consequent generation of more active metabolites, thus allowing once-daily application) are basic features in this respect, as exemplified by methylprednisolone aceponate (Topert 1988).

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