An Update on Topical Therapies for Mild-Moderate Psoriasis

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KEYWORDS

• Calcipotriol • Calcitriol • Corticosteroids • Ditranol • Small molecules • Tar • Tazarotene

KEY POINTS

- Current topical treatments are described in monotherapy and combination schedules.
- Evidence is available that the combination of calcipotriol and potent corticosteroids is more effective and has less side effects compared with monotherapies.
- Adherence is relevant for the success of a topical treatment.
- New small molecules provide opportunities for advances in new topical treatments of psoriasis.

GENERAL INTRODUCTION

Topical therapies are the first-line treatment in most patients with psoriasis.[1] In general treatments are given for short episodes. In patients who use systemic treatments or biologics, a topical treatment may be indicated for residual recalcitrant lesions. Combinations of several topicals or a topical and a systemic treatment is common practice.

Adherence to treatment may be a limitation of topicals. In particular if a treatment has a slow onset of efficacy or the treatment offers a practical problem, treatment adherence may seriously decrease the outcome.[2] Therefore, innovations in formulation of topicals may provide meaningful improvement in adherence.

The vehicle can have a therapeutic effect by itself. This is clearly shown in recent trials with the scalp lipogel containing calcipotriol and betamethasone dipropionate for scalp psoriasis, where response rates greater than 20% were achieved with the lipogel vehicle by itself without active ingredients.[3]

Evidence for efficacy is restricted for the classical topical treatments and more extensive for the first-line topical treatments.[4,5] Based on the best evidence and expert opinions treatment guidelines have been constructed.[6] This article highlights the current position of available topical agents and provides an insight into the future perspectives of small molecules.

THE CURRENT POSITION OF CLASSICAL TOPICAL AGENTS

The three classical topical therapies dithranol, tar, and salicylic acids have been used in the treatment of psoriasis for 50 to 100 years. Efficacy and safety studies at the highest level of evidence are sparse. Methods of classical treatments are not standardized and different protocols in different treatment settings are used. Therefore, the interpretation of studies comparing classical and more innovative topical results cannot be generalized.[7] When first-line topical treatments and systemic therapies are ineffective or contraindicated classical topicals may provide the solution.

Dithranol (anthralin, cignolin,1,8-dihydroxy-9-anthrone) has been available for nearly 100 years. It has a marked antihyperproliferative effect and inhibits mitogen-induced T-lymphocyte proliferation

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and neutrophil chemotaxis. In Europe and other regions outside the United States, it is used most often in daycare centers and the inpatient setting.[8] Efficacy of dithranol in patients with moderate to severe psoriasis at inpatient departments and at daycare units has been reported to be 66% and 81.7%, respectively.[9]

Coal tar has a range of anti-inflammatory actions and is effective as an antipruritic agent. Coal tar activates the aryl hydrocarbon receptor, resulting in induction of epidermal differentiation. It also counteracts Th2 cytokine-mediated downregulation of skin barrier proteins.[10] Although tar has been shown to induce skin cancers in animal experiments, coal tar has not been shown to be a carcinogenic risk factor if provided as a specific antipsoriatic treatment.[11]

THE CURRENT POSITION OF FIRST-LINE TOPICAL AGENTS

The evidence-based approach to estimate efficacy and safety of topical treatments is hampered because few randomly controlled trials are available for the classical topical treatments. Evidence-based data for corticosteroids are less than for vitamin D–based treatments and tazarotene.[12] Strategies containing potent corticosteroids (alone or in combination with a vitamin D analogue) or very potent corticosteroids have dominated the treatment progress for psoriasis on the trunk, limbs, and scalp. For treatment of the face and flexures calcineurin inhibitors and weak topical corticosteroids are indicated.

Guidelines of care for the management and treatment of psoriasis with topical therapies have been developed by the American Academy of Dermatology.[6]

Vitamin D_3 Analogues

In the early 1990s, vitamin D_3 analogues became commercially available as a topical treatment for psoriasis. Vitamin D_3 inhibits excess epidermal proliferation, and enhances cornified envelope formation; it also inhibits several neutrophil functions. Because of their therapeutic efficacy and limited toxicity, calcipotriol, calcitriol, and tacalcitol have become a first-line treatment in psoriasis.

Calcipotriol monotherapy can result in a 59% reduction of psoriasis area and severity index (PASI) after 8 weeks of treatment.[13] In up to 5% of patients irritation of the skin necessitates discontinuation of vitamin D treatments. Calcitriol is now a widely accepted vitamin D treatment in psoriasis.[14] In view of the moderate efficacy and irritation vitamin D treatments are often combined with a topical corticosteroids.

Corticosteroids

Since their introduction in the early 1950s, topical corticosteroids have become a mainstay in the treatment of psoriasis. They are first-line therapy in mild to moderate psoriasis and are effective in low-potency sites, such as the flexures and genitalia, where other topical treatments can induce irritation.

Over the years, the anti-inflammatory properties of topical corticosteroids have been improved by increasing their lipophilicity. For example, fluticasone propionate is very lipophilic because of its highly esterified structure.[15,16]

Corticosteroids are manufactured in various vehicles, from ointments, creams, and lotions to gels, foams, sprays, and shampoo.[16–18] Novel formulations provide additional options for individuals. Clobetasol propionate 0.05% spray allows application of corticosteroids on areas that are difficult to reach[19] and has been shown to be even more potent than the ointment formulation.[20]

Clobetasol propionate and betamethasone valerate in foam formulations are well appreciated by patients because drying is rapid with minimal residue left on the skin after application. Significant efficacy has been shown in placebo-controlled studies.[20–22] These formulations are also well suited for the treatment of scalp psoriasis. Clobetasol in a shampoo formulation is now available for the treatment of scalp psoriasis and has been shown to be superior to a tar-blend shampoo.[23]

Long-term treatment with the shampoo formulation using twice weekly applications proved to be effective and safe, with 66% and 79% of the patients reporting treatment satisfaction and user convenience, respectively.[24] Innovations in corticosteroid formulation are also provided by nail lacquers. In a small study of 10 patients, 8% clobetasol nail lacquer resulted in reduced onycholysis, pitting, and salmon patches after only 4 weeks of treatment.[25] This formulation is safe, effective, and cosmetically acceptable for the treatment of nail bed and matrix psoriasis, locations that are difficult to treat because drug penetration is traditionally poor in these areas.

Corticosteroids are highly effective in psoriasis when used continuously for up to 8 weeks and intermittently for up to 52 weeks. There is a lack of long-term efficacy and safety data available on topical interventions used for psoriasis. Unfortunately, no efficacy data are available on prolonged treatment for more than 3 months. Because tachyphylaxis and/or rebound can occur fairly rapidly (ie, within a few days to weeks), intermittent treatment schedules (eg, once every 2 or 3 days or on