Topical Treatments

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Introduction

Psoriasis is a chronic inflammatory skin disease that affects 2–4% of the world's population. Approximately 80% of psoriasis patients have limited, localized mild-to-moderate disease where topical therapies serve as the mainstay of treatment. Topical therapies can provide both high efficacy as well as safety in this population. Furthermore, in patients with moderate-to-severe disease, short-term topical treatments may provide symptomatic relief, minimize doses of photo- or systemic therapy, and be of benefit for resistant lesions as part of a combination regimen. The aim of this chapter is to provide an evidence-based concise overview of the available topical treatments for chronic plaque psoriasis.

Topical Corticosteroids

Topical corticosteroids are the primary treatment option for psoriasis in the United States. At least three out of four psoriasis patients are treated with topical corticosteroids [1]. When individualized appropriately to a patient, they are fast-acting, highly effective, and relatively safe compared to other types of therapies (e.g., photo-, systemic, and biologic therapies). There are a great number of topical corticosteroid agents that can be categorized by potency, formulation (e.g., creams, ointments, lotions, sprays, etc.), or the combination of active agents (e.g., betamethasone plus calcipotriene). Thus, understanding the subtle yet dynamic differences of topical corticosteroid potencies and formulations can translate into flexibility and maximum therapeutic benefit to patients.

Mechanism of Action and Pharmacology

The mechanism of action of corticosteroids is both specific and nonspecific and involves modulation of the skin at multiple levels, including anti-inflammatory, immunosuppressive, vasoconstrictive, and antiproliferative effects. The pharmacological effects of topical and systemic corticosteroids are overall similar but differ in the amount of the effective dose of the drug delivered to the target organ and the enhanced effect of systemic corticosteroids

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on suppressing recruitment of immune cells from the blood and bone marrow [2]. Generally, topical corticosteroids have three essential abilities in the treatment of psoriasis: (1) suppression of localized immune response through local reduction in cytokines, (2) vasodilatory effects, and (3) slowing hyperproliferation of keratinocytes.

A corticosteroid is a fat-soluble molecule that can freely diffuse through the cell membrane and bind to a corticosteroid receptor in the cytoplasm. This complex of corticosteroid and its receptor then enters the nucleus where it alters gene transcription and expression of mRNA. This process leads to alteration in protein expression, including decrease in the production of cytokines (e.g., interleukin [IL]-1, IL-2, IL-6, and interferon [IFN]-α) [3]. Corticosteroids also decrease the production of key vasodilatory substances and consequently lead to vasoconstriction [4]. The ability of corticosteroids to decrease cytokines and vasodilatory substances lead to suppression of localized inflammation and further immune cell recruitment. The antiproliferative effect of topical corticosteroids is mediated by inhibition of DNA synthesis and mitosis and is known to reduce keratinocyte size and proliferation [5].

Topical corticosteroids are made in several formulations with varying potency that are appropriate for use in certain body sites. In the United States, the potency of corticosteroids is scaled I to VII in the Stoughton-Cornell classification based on their ability to cause vasoconstriction [6]. Table 2.1 summarizes the topical corticosteroids available in the United States by potency. While the potency of systemic corticosteroids generally translates into predictable clinical results dependent on their route of administration (e.g., oral or intramuscular injection), topical corticosteroids must penetrate the stratum corneum to reach their target cells. The penetration of the stratum corneum varies according to the body site due to differences in skin thickness and the vascular supply to the area. For example, inflamed, moist, or denuded skin areas have greater penetration than the skin of the scalp, palms, and soles. Therefore, while the inherent potency of topical corticosteroids is ranked based on their vasoconstrictive properties, this does not necessarily accurately predict the ability of a formulation to deliver the medication to a target area. Furthermore, in addition to the skin barrier, the potency of topical corticosteroids is also affected by its chemical modification, its vehicle formulation, and its application (e.g., patient compliance and application with or without occlusion) (see Special Considerations below).

Efficacy

Superpotent (class I) topical corticosteroids are well established for effective treatment of mild-to-moderate plaque psoriasis [7–10]. Katz et al. showed that clobetasol-17-propionate and betamethasone dipropionate are effective in clearing or markedly improving psoriasis in 75–80% of patients after approximately 3 weeks [11]. Blum et al. demonstrated rapid onset of efficacy of halobetasol propionate 0.05% occurring within 5 days of initiating treatment. There was also clearance or marked improvement in 88% of patients over the course of 4 weeks compared to 64% of patients treated with betamethasone valerate [9]. Studies on the use of highly potent (class II) topical corticosteroids showed less efficacy in that only an average of 50% of patients achieved at least 75% improvement and less than 10% achieved clearance [8, 12, 13, 14].

Betamethasone dipropionate spray (Sernivo™) is a new mid-potent (class IV) formulation of betamethasone dipropionate 0.05% that has been recently approved for the treatment of mild-to-moderate psoriasis in 2016. When assessed using the Investigator's Global Assessment (IGA) and Total Severity Score (TSS) in phase III clinical trials, betamethasone dipropionate spray showed equivalent efficacy to augmented, superpotent formulation (lotion) of betamethasone dipropionate 0.05% and superiority to vehicle at day 15 (19% versus 18.9% and 2.3%, respectively) [15, 16]. These studies also showed superiority of this new medication in terms of its faster onset of action in improving erythema and scaling by day 4. Furthermore, improvements were also seen in locations that are typically difficult to treat such as the knees and elbows. The mid-potency designation suggests its superiority in safety and limited systemic absorption compared to superpotent topical corticosteroids.

Table 2.1 Topical corticosteroids available in the United States

Potency	Corticosteroid	Vehicle form	Trade name (United States)
Class I (superpotent)	Betamethasone dipropionate, augmented	Ointment	Diprolene
		Lotion	Diprolene
		Gel	Diprolene
	Clobetasol propionate	Ointment	Temovate
		Lotion	Clobex
		Gel	Temovate
		Cream	Temovate
		Cream, emollient based	Temovate E
		Foam, aerosol	Olux-E
		Foam, aerosol (scalp)	Olux
		Shampoo	Clobex
		Solution (scalp)	Temovate, Cormax
		Spray (aerosol)	Clobex
	Fluocinonide	Cream	Vanos
	Flurandrenolide	Tape (roll)	Cordran
	Halobetasol propionate	Ointment	Ultravate
		Lotion	Ultravate
		Cream	Ultravate
Class II (high potency)	Amcinonide	Ointment	Cyclocort[a], Amcort[a]
	Betamethasone dipropionate	Ointment	Diprosone
		Cream, augmented	Diprolene, augmented
	Desoximetasone	Ointment	Topicort
		Gel	Topicort
		Cream	Topicort
	Diflorasone diacetate	Ointment	ApexiCon[a], Florone[a]
		Cream, emollient	Apexicon E
	Fluocinonide	Ointment	Lidex[a]
		Gel	Lidex[a]
		Cream, anhydrous	Lidex[a]
		Solution	Lidex[a]
	Halcinononide	Ointment	Halog
		Cream	Halog
Class III (high potency)	Amcinonide	Lotion	Amcort[a]
		Cream	Cyclocort[a], Amcort[a]
	Betamethasone dipropionate	Cream, hydrophilic ointment	Diprosone
	Betamethasone valerate	Ointment	Valisone[a]
		Foam	Luxiq
	Desoximetasone	Cream	Topicort
	Diflorasone diacetate	Cream	Florone[a]
	Fluocinonide	Cream aqueous emollient	Lidex-E[a]
	Fluticasone propionate	Ointment	Cutivate
	Mometasone furoate	Ointment	Elocon
	Triamcinolone acetonide	Ointment	Kenalog[a]
		Cream	Triderm, Aristocort HP[a]

(continued)

Table 2.1 (continued)

Potency	Corticosteroid	Vehicle form	Trade name (United States)
Class IV (medium potency)	Betamethasone dipropionate	Spray	Sernivo
	Clocortolone pivalate	Cream	Cloderm
	Fluocinolone acetonide	Ointment	Synalar[a]
	Flurandrenolide	Ointment	Cordran
	Hydrocortisone valerate	Ointment	Westcort
	Mometasone furoate	Lotion	Elocon
		Cream	Elocon
		Solution	Elocon[a]
	Triamcinolone acetonide	Ointment	Kenalog[a]
		Cream	Kenalog[a]
		Aerosol spray	Kenalog
Class V (lower-mid-potency)	Betamethasone dipropionate	Lotion	Diprosone
	Betamethasone valerate	Cream	Beta-Val, Valisone[a]
	Desonide	Ointment	DesOwen, Tridesilon[a]
		Gel	Desonate
	Fluocinolone acetonide	Cream	Synalar[a]
	Flurandrenolide	Lotion	Cordran
		Cream	Cordran
	Fluticasone propionate	Lotion	Cutivate
		Cream	Cutivate
	Hydrocortisone butyrate	Ointment	Locoid
		Lotion	Locoid
		Lotion, spray	Cortizone 10 maximum
		Cream	Locoid, Locoid Lipocream
		Solution	Locoid
	Hydrocortisone probutate	Cream	Pandel
	Hydrocortisone valerate	Cream	Westcort[a]
	Prednicarbate	Ointment	Dermatop
		Cream, emollient	Dermatop
	Triamcinolone acetonide	Ointment	Kenalog[a]
		Lotion	Kenalog[a]
Class VI (low potency)	Aclometasone dipropionate	Ointment	Aclovate
		Cream	Aclovate
	Betamethasone valerate	Lotion	Beta-Val, Valisone
	Desonide	Lotion	DesOwen, Tridesilon
		Cream	DesOwen, LoKara
		Foam	Verdeso
	Fluocinonide acetonide	Cream	Synalar[a]
		Shampoo	Capex
		Solution	Synalar[a]
		Oil (scalp)	Derma-Smoothe/FS
		Oil (body)	Derma-smoothe/FS
	Triamcinolone acetonide	Lotion	Kenalog[a]
		Cream	Kenalog[a], Aristocort[a]

(continued)

Table 2.1 (continued)

Potency	Corticosteroid	Vehicle form	Trade name (United States)
Class VII (least potent)	Hydrocortisone (base, ≥2%)	Ointment	Hytone
		Lotion	Hytone, ala scalp, Scalacort
		Cream	Hytone[a], Nutracort[a]
		Solution	Texacort
	Hydrocortisone (base, <2%)	Ointment	Cortaid, Hytone, Nutracort
		Lotion	Aquanil HC, Sarnol-HC, Cortizone 10
		Cream	Cortaid, Hytone, Synacort
		Solution	Cortaid, Noble, scalp relief
		Spray	Cortaid
	Hydrocortisone acetate with pramoxine 1% combination	Ointment	Pramosone
		Lotion	Pramosone, Analpram-HC
		Cream	Pramosone, Analpram-HC
		Aerosol foam	Epifoam

[a]Inactive US trade name; the brand may be available outside the United States

Special Considerations

The choice of vehicle can significantly affect the use and penetration of topical corticosteroids and therefore translates to differences in efficacy. Patient compliance to topical therapy can be positively or negatively impacted depending on the topical agent's esthetic appeal. There are numerous types of vehicles including ointment, lotion, cream, shampoo, gel, solution, spray, foam, oil, and tape (see Table 2.1). Different vehicles are indicated for different body sites, but the optimal choice will generally be the vehicle that the patient is most likely to use (e.g., a patient may have a different preference of vehicle [shampoo, gel, solution, spray, or foam versus cream or ointment] for psoriasis on the scalp).

Occlusion of topical corticosteroids can also alter the penetration, thereby altering the effectiveness. For example, a lower-mid-potent (class V) topical corticosteroid, flurandrenolide 0.1%, has been shown to act as a superpotent topical corticosteroid when applied with tape [8].

Application

Generally, for thick psoriasis plaques on the extensor surfaces, super- or high-potency topical corticosteroids (e.g., betamethasone 0.05% or clobetasol propionate 0.05%) are needed. Low-potency cream (e.g., hydrocortisone 1%) is suitable for the face and intertriginous areas.

Table 2.2 Side effects of topical corticosteroids

Cutaneous	Systemic
Irritation	HPA axis suppression
Burning	Cushing syndrome
Pruritus	Glaucoma
Atrophy of the skin	
Striae	
Telangiectasia	
Acneiform eruption	
Rosacea	
Perioral dermatitis	
Folliculitis	
Infection (bacterial, fungal)	
Contact dermatitis	
Hypopigmentation	
Purpura/ecchymoses	
Folliculitis	
Rebound of psoriasis	
Tachyphylaxis	

Side Effects

The risk of cutaneous and systemic side effects associated with long-term topical corticosteroid use increases with higher potency formulations (see Table 2.2). Thus, it is important to avoid

excessive frequency, duration, or application of topical corticosteroids to sensitive areas such as the face or intertriginous areas.

Vitamin D Analogs

The vitamin D analogs include calcitriol and its synthetic derivatives calcipotriene (also called calcipotriol) and tacalcitol. Of these, only calcipotriene and calcitriol are available in the United States. Calcitriol is only available in ointment form, while calcipotriene can be found in solution, cream, ointment, foam, and gel suspension formulations. Calcipotriene is also available in combination with betamethasone in ointment, suspension, or foam formulations.

Mechanism of Action and Pharmacology

Although the mechanism of action of vitamin D analogs is not completely known, binding of these analogs to vitamin D receptors leads to inhibition of keratinocyte proliferation and enhancement of keratinocyte differentiation [17, 18]. In addition, vitamin D analogs have immunosuppressive properties including inhibition of production of several proinflammatory cytokines, including IL-2 and IFN-γ, that may be equally important to their anti-psoriatic effects [19, 20].

Vitamin D analogs are often used in combination with other topical agents including halobetasol propionate, tazarotene, and crude coal tar to maximize efficacy while reducing the risk of skin atrophy that is associated with chronic corticosteroid use [21, 22]. However, calcipotriene is a relatively unstable molecule that is inactivated by acidic substances, and as such, it is not compatible with some topical therapies used in psoriasis treatment such as salicylic acid. It is also known to be degraded to some extent in the presence of hydrocortisone valerate and ammonium lactate.

Efficacy

In randomized controlled trials, calcipotriene was found to be at least as effective as calcitriol, potent topical corticosteroids, hydrocortisone 0.5%, and coal tar [23]. Calcipotriene cream is less efficacious than ointment with efficacy comparable to betamethasone valerate and coal tar derivatives. However, many patients prefer to use the cream formulation on the body, and there is some evidence that patients are more likely to adhere to use of calcipotriene twice daily if they alternate between cream in the morning and ointment in the evening [24]. Monotherapy with calcipotriene foam is efficacious and is the preferred vehicle of calcipotriene in scalp psoriasis, with 40.9% of patients achieving clear or almost clear scalp after 8 weeks [25].

Side Effects

Skin irritation is the most common side effect of vitamin D analogs. This usually presents as lesional or perilesional burning, stinging, erythema, or scaling. Hypercalcemia is the only serious concern with the use of topical vitamin D preparations; however, this risk is minimized when using less than the recommended weekly maximum of 100 g of calcipotriene [26].

Combination Preparations with Corticosteroids

While mixing vitamin D analogs and corticosteroids is not always possible (due to the degradation of calcipotriene by some steroids as mentioned above), there are currently three stable combination preparations available in the United States: calcipotriene and betamethasone dipropionate ointment and suspension (Taclonex®) and calcipotriene and betamethasone dipropionate foam (Enstilar®).

The ointment, suspension, and foam preparations all contain calcipotriene 0.005% (equivalent to 50 μg/g) and betamethasone dipropionate 0.064% (equivalent to betamethasone 0.5 mg/g)

and are indicated for the treatment of psoriasis in adults for up to four consecutive weeks [27]. When applied twice daily for 4 weeks, the combination ointment led to a greater mean Psoriasis Area and Severity Index (PASI) reduction (74.4%) than the individual components applied twice daily (betamethasone dipropionate 61.3% and calcipotriene ointment 55.3%) [28]. Once daily application of the combination ointment, which has been shown to lead to greater patient compliance than twice daily application, produced mean PASI reduction of 69–71% over 4 weeks [28, 29, 30].

The once daily application of the combination foam significantly reduced the mean modified PASI (mPASI) scores compared to once daily application of either individual component of calcipotriene or betamethasone foam alone (71% mean reduction versus 42% and 55%, respectively). Once daily application of the combination foam also achieved significantly greater PASI-75 response (≥75% improvement from the baseline PASI score) than either calcipotriene or betamethasone alone (49% versus 18% and 34%, respectively) [31]. The combination foam is efficacious not only on the body but also on the scalp. Compared to a gel formulation used for 8 weeks, the foam formulation of calcipotriol and betamethasone was more efficacious after just 4 weeks of treatment with a PASI-75 response rate of 52% versus 35% and a PASI-90 response rate of 22.2% versus 10.7% [32]. Furthermore, a greater proportion of patients using the foam reported that it was easier to apply and preferred it to their previous topical regimens. Once daily use of the foam formulation was more effective than the calcipotriol/betamethasone combination ointment in terms of treatment success rate and mPASI improvement (54.6% versus 43.0%). However, the PASI-75 and PASI-50 response rates were not statistically different between the foam versus ointment [33].

Based on above, the combination of a vitamin D analog and betamethasone dipropionate applied either once or twice daily in either ointment or foam vehicle appears to have superior efficacy compared to either component of the combinations applied as monotherapy.

Tazarotene

Tazarotene (Tazorac®) is a topical retinoid that was approved for treatment of psoriasis in 1997. It is available as a 0.1 and 0.05% gel and cream. While approved for use as a single agent, patients can often experience minimal effectiveness and significant local skin irritation that limits its use. The combination of this agent with other therapies (e.g., topical corticosteroids) has been used to minimize irritation and to increase efficacy, which has allowed tazarotene to become part of a long-term combination maintenance regimen. Tazarotene has also been used with ultraviolet (UV) B therapy for more rapid improvement, increased efficacy, and lower cumulative UV dosage exposure.

Mechanism of Action and Pharmacology

Tazarotene is a vitamin A-derived acetylene retinoid that selectively binds to the retinoic acid receptors (RARs) β and γ [34]. The active metabolite, tazarotenic acid, binds to RARs that leads to alteration of gene expression. The precise mechanism of action in psoriasis is unclear but may be related to both anti-inflammatory and antiproliferative actions (e.g., inhibition of transglutaminase expression and keratin 16 expression) [35].

A study by Hecker et al. demonstrated that tazarotene exhibits minimal degradation in vitro (<10%) when combined with a variety of topical corticosteroids and with calcipotriene [22]. It also did not appear to affect the stability of other compounds. A similar in vivo study analyzing tazarotene with these topical products in combination is needed.

Efficacy

Tazarotene gel at both 0.1 and 0.05% concentrations applied once daily has been shown to be similar in efficacy to fluocinonide 0.05% cream [36]. In one study, tazarotene 0.1% gel applied as a single agent once daily resulted in 70% of

patients reaching the clinical endpoint of treatment success (≥75% improvement from baseline), with 41% maintaining significant improvement 12 weeks after stopping the drug [34]. When combining tazarotene with intermediate and superpotent topical corticosteroids, more rapid improvement, improved efficacy, and decreased irritation have been reported [37–39]. Combination of tazarotene and corticosteroids may also prevent atrophy [40, 41]. When combining tazarotene with calcipotriene, Bowman et al. showed comparable efficacy to clobetasol dipropionate 0.05% ointment [42]. Tazarotene has also been successfully combined with broadband and narrowband UVB for more rapid and effective clearing of psoriasis compared to either treatment alone [43–45].

Application

As monotherapy, tazarotene should be applied directly on the thick and scaly psoriatic lesions and the surrounding unaffected skin should be avoided. Application of tazarotene to sensitive areas such as the face and the neck may easily cause irritation. Genital areas should be avoided for the same reason. If significant irritation occurs, decreasing the frequency of application, starting at the lower 0.05% concentration and increasing the concentration as tolerated, switching formulations (e.g., gel to cream), or utilizing the "short-contact" method may be of benefit (Table 2.3) [46].

Side Effects

Application of tazarotene may lead to teratogenic systemic concentrations if applied to more than 20% of the total body surface area [47]. Therefore, women of childbearing potential must be cautioned of the risk before starting treatment. Adequate birth control measures must be utilized while on therapy.

Adverse local effects include a burning and stinging sensation, as well as peeling, erythema, and localized edema of the skin. This sensitivity occurs more commonly with the 0.1% concentration compared to 0.05% [46]. Burns and photosensitivity are of concern in those receiving UVB phototherapy and taking photosensitizing medications, respectively [50]. These patients should be cautioned to minimize sunlight exposure and to use sunscreens and protective clothing.

Table 2.3 Tazarotene short-contact therapy

Apply tazarotene to plaques for a short time (5–20 min)
Wash medication off with water after prescribed time period
Gradually increase application time by 1–5 min as tolerated

Calcineurin Inhibitors (Tacrolimus and Pimecrolimus)

Topical calcineurin inhibitors, tacrolimus 0.1% (Protopic®) and pimecrolimus 1% (Elidel®), have been shown to be effective in the treatment of psoriasis [48–51]. However, they are not officially FDA approved for the treatment of psoriasis and are commonly used off-label. Their use can be of benefit particularly in areas where topical corticosteroids should ideally be avoided (e.g., facial and intertriginous areas). Tacrolimus and pimecrolimus are available as topical therapy in ointment and cream formulations, respectively.

Mechanism of Action and Pharmacology

The mechanism of action of calcineurin inhibitors involves the reduction of T-cell proliferation through inhibition of calcineurin, a calcium- and calmodulin-dependent phosphatase enzyme [51, 52, 53]. This process inhibits the translocation of a family of transcription factors called nuclear factor of activated T cells (NFAT), leading to reduced transcriptional activation of cytokine genes, including IL-2, IL-3, IL-4, TNF-α, and IFN-γ.

Efficacy

Topical tacrolimus and pimecrolimus are generally well-tolerated when used to treat facial and intertriginous psoriasis and allow avoidance of chronic topical steroid use in these sensitive areas. However, it appears to be less effective in other areas, which may be due to differences in absorption.

In a clinical trial with tacrolimus 0.1% ointment, twice daily application to facial and intertriginous psoriasis lesions resulted in more patients achieving clear or almost clear psoriasis compared to placebo (65% versus 32%) [54]. Furthermore, the addition of 6% salicylic acid to tacrolimus 0.1% ointment has been shown to produce greater improvement of plaques than tacrolimus alone [55].

In a clinical trial with pimecrolimus 1% cream, twice daily application resulted in more patients achieving clear or almost clear inverse psoriasis compared with placebo (71% versus 21%) [56]. However, compared to topical corticosteroids, pimecrolimus appears to be less effective [57].

Application

A thin layer of tacrolimus 0.1% ointment or pimecrolimus 1% cream can be applied to the psoriatic lesions twice daily. Patients should be instructed to rub the ointment/cream gently and completely to the affected area. Burning and stinging is most common in the first few days of application but generally improve as the lesions improve. Application should continue as long as signs and symptoms persist and discontinued if resolution occurs.

Side Effects

Tacrolimus ointment and pimecrolimus cream are commonly associated with burning and stinging, particularly tacrolimus. There is also a black box warning regarding the possible link between topical calcineurin inhibitors and cases of lymphoma and skin cancer [58]. No definite causal relationship has been established, and subsequent studies have not found an increased incidence of lymphoma [59, 60].

Anthralin (Dithranol)

Topical anthralin (also known as dithranol) has been used effectively in the treatment of psoriasis since the early twentieth century. Anthralin is a synthesized version of the natural product chrysarobin, which comes from the South American araroba tree. Due to problem of staining and irritancy, anthralin has not been widely used as a first-line agent in treating psoriasis. Rather, it has been most commonly used in treating localized psoriasis plaques resistant to other therapies. It is approved for the treatment of chronic plaque-type psoriasis in the United States and is available as 1% and 1.2% creams and as a 1% shampoo.

Mechanism of Action and Pharmacology

Anthralin inhibits monocyte proinflammatory activity and induces extracellular generation of reactive oxygen species [61]. It also has an anti-Langerhans cell effects [62]. However, the precise mechanism of action of anthralin in psoriasis is not completely known. Its actions include the inhibition of DNA synthesis and a decrease in the mitotic rate of epidermal cells in psoriasis [63]. Anthralin also suppress the IFN-γ-induced upregulation of cytokeratin 17, which may be implicated in the pathogenesis of psoriasis [64].

Efficacy

Anthralin is typically used for short durations. Approximately 30% of psoriasis patients achieve clearance after an average of 5 weeks [65–67]. The efficacy of anthralin is increased when used in combination with other therapies.

Application

The adverse effects of anthralin, the permanent red-brown staining of clothing, and the temporary staining of the skin have limited the use of anthralin in the United States. As a result, the "short-contact anthralin therapy (SCAT) is often used in the outpatient setting where 1% or 1.2% anthralin is applied for 5–10 min per day." Subsequently, the application time is titrated up to 20–30 min as tolerated.

Side Effects

Skin irritation is a common side effect of anthralin and includes contact dermatitis, erythema, edema, and temporary staining of the hair, nails, and skin.

Salicylic Acid

Salicylic acid is a keratolytic agent that has been commonly used for the treatment of mild-to-moderate psoriasis for years. Its mechanism of action in psoriasis involves desquamation of hyperkeratotic epithelium via dissolution of the intercellular cement which causes thinning and scaling of the plaques [68]. Its use is limited as monotherapy since it only removes scales in the treatment of psoriasis. More commonly, salicylic acid is used as an adjunct to other topical medications. Although not commercially available as a compound with other types of topical agents, salicylic acid has been shown to increase the penetration and efficacy of topical corticosteroids, and the combination is overall more effective than either agent alone [69]. Salicylic acid can be used for the treatment of psoriasis as a 6% gel or shampoo and works well in combination with other psoriasis therapies including topical corticosteroids and coal tar. Of note, salicylic acid inactivates calcipotriol upon contact and blocks UVB; thus, it should not be used with calcipotriol or prior to UVB phototherapy [70]. Side effects of salicylic acid, such as tinnitus and fatigue, can occur if applied to >20% of the body surface area [76]. While rare, cases of hypoglycemia in diabetic patients have also been reported following the application of salicylic acid over a large surface area [76].

Coal Tar

Coal tar is the ancient modality of treating psoriasis, although its popularity has decreased since the development of newer and less messy topical treatment options. While long-existed as a treatment option for psoriasis, its mechanism of action is uncertain due to the countless ingredients in coal tar. However, clinically, it provides antipruritic, anti-inflammatory, and anti-psoriatic effects [71]. Coal tar can be found in several preparations, including ointment, lotion, cream, shampoo, gel, solutions, and soaps in multiple concentrations. Crude coal tar used in Goeckerman therapy includes 2, 5, and 10% concentrations. The Goeckerman therapy was first developed in 1925 and involves the application of crude coal tar to the entire body, including unaffected areas, for several hours a day along with UVB therapy.

Lactic Acid

Lactic acid is a less commonly used keratolytic agent for the treatment of psoriasis. This is an effective and useful second-line keratolytic agent when salicylic acid is not an option. It is commonly used in diabetic patients when salicylate toxicity is a concern. It has been shown that hairless mice exhibit increased desquamation of normal skin when this agent is applied [72].

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