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Commentary

Are topical keratolytic agents needed in the treatment of scalp psoriasis?

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Abstract

Background: Topical corticosteroids are the primary treatment for scalp psoriasis. Keratolytic agents are promoted as adjunctive treatments. However, complex treatment regimens may result in poor adherence and outcomes.

Objective: To evaluate the evidence for the need for use of topical keratolytic agents as opposed to topical corticosteroid monotherapy in the treatment of scalp psoriasis.

Methods: A review of the literature was performed seeking clinical trials using topical keratolytics, topical corticosteroids or the combination for treatment of scalp psoriasis.

Results: Complete clearance of scalp psoriasis can be achieved in 10-78% of patients using topical corticosteroids alone, in 3% of patients using topical keratolytics alone, and in up to 84% using a combination of topical keratolytics and topical steroids. Clinical trials comparing the combination of keratolytics and topical corticosteroids versus topical corticosteroids alone found marginally more efficacy using combination regimens.

Limitations: We could not find any long term study evaluating the efficacy of combination therapy in scalp psoriasis and its effect on the patients' adherence.

Conclusion: High potency topical corticosteroids are usually effective in treating scalp psoriasis in clinical trials. Poor efficacy in clinical practice may be owing to poor adherence to the treatment regimen. Using a keratolytic agent in conjunction with a topical corticosteroid may provide marginal additional benefit in clinical trials, but that benefit is likely outweighed by the downside of complicating treatment and reducing adherence in the clinical setting, unless a single product containing both medications were used.

Key words: keratolytic, salicylic acid, steroid, corticosteroid, glucocorticoid, clobetasol, betamethasone, psoriasis, scalp, treatment

Introduction

Scalp psoriasis and its treatment are considerably frustrating for patients and often for dermatologists as well. Numerous treatments have been recommended, likely indicative of how poorly any one treatment works. Topical treatment regimens usually consist of topical corticosteroids (often a super high potency product such as clobetasol propionate), supplemented with a topical

vitamin D product, keratolytics, and/or medicated shampoo products. [1,2,3,4,5,6,7]. Many of the suggested treatments can be quite messy and difficult to use [3,8]. Given the difficulty of applying medicines to hair bearing areas, poor adherence to treatment may be a primary factor for poor scalp psoriasis treatment outcomes [3,8,9,10,11].

Keratolytic agents such as salicylic acid may be recommended to promote the shedding of psoriatic scales, theoretically facilitating greater penetration of topical medication [12,13,14,15,16]. However, the need for such facilitation is unclear because normal scalp skin has low barrier function to percutaneous absorption of topical drugs and barrier function is further reduced in diseased skin [17]. Even thick-plaque rupioid psoriasis may respond rapidly to topical steroids [18]. Moreover, some studies show no increase in penetration of corticosteroids using kerstolytics [19].

A major factor complicating the treatment of scalp psoriasis is poor adherence to prescribed treatment regimens [10,20,21]. Given that topical medications should easily penetrate psoriatic scalp lesions and given the tendency toward poor adherence with complex topical regimens, the use of keratolytic agents may not provide additional clinical benefit in practice. A review of the literature was performed in order to determine whether adding topical keratolytic agents to topical corticosteroids attained improved clinical outcomes compared to treatment with topical corticosteroids alone.

Methods

In this article, we sought to review the literature on the efficacy of topical keratolytics in the treatment of scalp psoriasis and the additive effects these agents might provide with the use of topical steroids,. We searched Medline for articles published through December 2012. The search was performed using the terms (“keratolytics”, “keratolytic”, “salicylic”, “acid”, “urea”, “steroid”, “corticosteroid”, “glucocorticoid”, “clobetasol”, or “betamethasone”) and (“psoriasis” and “scalp”). Studies utilizing topical corticosteroids, topical keratolytics, or a combination of both agents were included. Reference sections of the reviewed articles were cross-referenced for studies regarding “keratolytic agents” used along with corticosteroids.

Results

Of 175 studies initially recovered, 23 studies were relevant and included. Fifteen studies utilized topical corticosteroids alone (Table 1); three studies used only keratolytic agents (Table 2); and 5 studies utilized a combination of topical keratolytics and topical corticosteroids (Table 3).

Complete clearance of scalp psoriasis can be achieved in 10% of patients using short contact topical corticosteroids alone in shampoo form, in 19-78% of patients using leave-on topical corticosteroids alone [13,22,23,24,25,26,27], in 3% of patients using topical keratolytics alone [28], and in up to 84% of patients using a combination of topical keratolytics and topical corticosteroids [13,14].

Clinical trials comparing a combination of keratolytics and topical steroids versus topical steroids alone found more efficacy using combination regimens with no increase in adverse effects [13,14,29,30]. However, the higher efficacy of combination therapy was statistically significant only in one study that used two different corticosteroids in treatment groups [14]. We found only one trial comparing a combination of a topical keratolytic and a topical corticosteroid versus the same corticosteroid alone. This study was a randomized double blind clinical trial including 22 patients with scalp psoriasis, 17 patients with scalp seborrheic dermatitis, and one patient with scalp neurodermatitis. In this study, combination therapy was marginally but not significantly more effective in reducing erythema, scaling, and pruritus at week 2-3 [29]. The study period was four weeks or less in all of the included comparative trials.

Table 1. Studies evaluating effects of topical corticosteroids in scalp psoriasis

Author	Number of patients	Methods	Outcome
Poulin Y et al.[31]	288	Patients with moderate to severe scalp psoriasis received once daily clobetasol propionate 0.05% shampoo treatment for up to 4 weeks.	78% of patients was clear or had mild disease after 4 weeks.

Poulin Y et al.[32]	168	Patients with moderate scalp psoriasis received once daily clobetasol propionate 0.05% shampoo treatment for up to 4 weeks.	84% of patients was clear or had mild disease after 4 weeks.
Bovenschen HJ et al.[33]	56	Patients with scalp psoriasis were treated with clobetasol propionate 0.05% shampoo once daily for 4 weeks. Efficacy and patient satisfaction were assessed using postal questionnaires.	Positive treatment satisfaction was reported by 66% of patients. Patient-rated indicators for disease severity improved by 39-46%.
Tan J et al.[34]	288	Patients with scalp psoriasis received once daily treatment with clobetasol propionate 0.05% shampoo for up to 4 weeks.	The percentage of participants who experienced none or mild scaling increased from 0.7% at baseline to 65% at week 4.
Griffiths CE et al.[35]	121	Patients with scalp psoriasis received once daily clobetasol propionate 0.05% shampoo treatment for up to 4 weeks.	The mean area involved fell from 48% at baseline to 29% after 4 weeks
Jarratt M et al. [22]	142	Patients with severe scalp psoriasis received once daily clobetasol propionate 0.05% shampoo treatment for up to 4 weeks.	At week 4, one third of patients were cleared or almost cleared, while 10% were completely cleared.
Sofen H et al.[27]	41	Patients with moderate-to-severe psoriasis of the scalp were treated with clobetasol propionate 0.05% spray twice daily for up to 4 weeks.	51% of patients cleared. 85% of patients achieved success (clear or almost clear).
Mazzotta A et al.[36]	12	Patients with scalp psoriasis applied clobetasol propionate 0.05% foam twice daily for 4 weeks.	At week 4, 100% of patients achieved improvement of the Psoriasis Area And Severity Index (PASI) score from baseline $\geq 50\%$ (PASI-50), while 58% demonstrated PASI-75.
Olsen EA et al.[26]	188	Clobetasol propionate 0.05% scalp lotion was used in patients with moderate to severe scalp psoriasis, twice-daily for 2 weeks	At the end of therapy, 81% of patients had 50% improvement or greater of their scalp psoriasis. Complete clearing was seen in 26% of patients.
Lassus A[25]	53	Patients with moderate to severe psoriasis of the scalp used a 0.05% solution of clobetasol propionate once-	At the end of the study, clearance was achieved in 19% and 78% of patients treated once-

Feldman SR et al.[37]	79	Patients with moderate to severe scalp psoriasis were treated with betamethasone valerate foam either once a day or twice a day for four weeks	daily or twice-daily for 2 weeks. There was 52% improvement in psoriasis severity with once daily and 61% improvement with twice daily therapy. The difference was not statistically significant.
Duweb GA et al.[38]	18	Patients with scalp psoriasis received twice-daily betamethasone valerate lotion for 6 weeks.	Marked improvement and clearance was achieved in 72% of patients.
Klaber MR et al.[24]	234	For treatment of scalp psoriasis, betamethasone valerate solution (1 mg/ml) was applied twice daily for 4 weeks.	At the end of treatment, the proportion of patients who had 'cleared' or 'markedly improved' was 75%. Complete clearance was achieved in a quarter of the patients.
Jemec GB et al.[39]	1097	Patients with scalp psoriasis received once-daily betamethasone dipropionate 0.5 mg/g scalp lotion or a combination of calcipotriene 50 µ/g plus betamethasone dipropionate 0.5 mg/g in the same vehicle for 8 weeks.	Clearance was achieved in 26% and "absent" or "very mild" disease in 64% of patients using betamethasone and in 34% and 71% respectively in the combination treatment group
Katz HI et al.[23]	193	Betamethasone dipropionate 0.05% lotion or clobetasol propionate 0.05% solution was used in the treatment of moderate-to-severe scalp psoriasis twice-daily for 2 weeks.	At the end of the study, clearance was achieved in 36% and marked improvement in 37% of patients treated with betamethasone. Clobetasol provided clearance in 25% and marked improvement in 45% of patients.
Lassus A[40]	40	Patients with moderate to severe psoriasis of the scalp used a 0.05% solution of clobetasol propionate or a 0.05% alcoholic solution of betamethasone dipropionate twice-daily for 2 weeks.	At the end of the study, erythema was resolved in 65% and 20% of patients treated with clobetasol or betamethasone, respectively.

Table 2. Studies evaluating effects of topical keratolytics in scalp psoriasis

Author	Number of	Methods	Outcome
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patients

Seité S et al.[41]	49	Patients with mild-to-moderate scalp psoriasis of the scalp used a shampoo containing 0.1% lipohydroxyacid and 1.3% salicylic acid every other days for 4 weeks.	There was 16% improvement in severity of disease.
Kircik L[12]	10	Salicylic acid 6% emollient foam was used twice-daily for 4 weeks in patients with scalp psoriasis.	60% of subjects were either "completely cleared" or "almost cleared" (~90% improvement) of their psoriasis by week 4. No adverse events were reported.
Going SM et al.[28]	30	Severe scalp psoriasis was treated with daily applications of 6% salicylic acid gel for 3 to 6 weeks.	Scalp psoriasis improved in 73% and cleared in 3% of patients. Side-effects were drying and stinging of the scalp in 20% of patients and hand irritation in 10% of patients.

Table 3. Studies evaluating effects of combination of topical keratolytics and topical corticosteroids in scalp psoriasis

Author	Number of patients	Methods	Outcome
Høvdning G et al.[15]	38	Patients with psoriasis of the scalp, were treated with a lotion containing 0.05% betamethasone dipropionate and 2% salicylic acid twice daily for 4 weeks	79% of patients were free of scaling after 4 weeks.
Ross SD et al.[30]	20	Patients with psoriasis of the scalp used 10% salicylic acid in mineral oil or a combination of 6% salicylic acid + 2% coal tar + 0.05% fluocinonide in gel base once daily for 3 days.	At 72 hours, there was 40% improvement in psoriasis severity with 10% salicylic acid and 52% improvement with combination therapy. The difference was not statistically significant.
Hillström L et al.[14]	40	A double-blind comparison was made between 0.25% desoxymethasone plus 1% salicylic acid solution versus 0.1% betamethasone valerate solution in patients with psoriasis of the scalp. Both preparations were	After 2 weeks, 65% of the patients in the desoxymethasone plus salicylic acid group and 30% in the betamethasone group were free of erythema. The difference was statistically significant. No adverse reaction was seen.

used twice daily for 2 weeks.

Hillström 53
L et
al.[13]

A double-blind comparison was made between 0.05% betamethasone dipropionate plus 2% salicylic acid solution versus clobetasol propionate lotion in patients with psoriasis of the scalp. Both preparations were used twice daily for 3 weeks.

After 3 weeks, 84% of the patients in the betamethasone plus salicylic acid group and 60% in the clobetasol group were cleared. No significant difference in efficacy was demonstrated. Two patients in the clobetasol group, and one in the betamethasone plus salicylic acid group experienced pruritus or folliculitis.

Elie R et 40
al.[29]

In a double-blind randomized trial, patients with erythematous squamous dermatoses (including psoriasis and seborrheic dermatitis) of the scalp were treated with a lotion containing either 0.05% betamethasone dipropionate, 2% salicylic acid, or 0.05% betamethasone dipropionate + 2% salicylic acid twice daily for 3 weeks.

Combination of topical corticosteroids and keratolytics was more effective than either drug alone. However, superiority of combination treatment over betamethasone alone was statistically significant only in regard to reduction in scaling at day 7. No adverse effects were observed in the study.

Discussion

Scalp psoriasis is a chronic disease that may require long-term application of topical therapies for adequate control. Highly potent preparations of topical corticosteroids are usually effective in controlling scalp psoriasis, at least in short term clinical trials [7,13,14,22,23,24,25,26,27,31,32,33,34,35,36,37,38,40,42]. In clinical practice, however, scalp psoriasis appears to be a form of disease that is highly resistant to treatment. The apparent resistance is not well explained by poor penetration because even normal scalp has barrier function similar to the axilla and diseased skin should permit even greater penetration of topical agents.

Because of the frustrating difficulties in scalp psoriasis management, complex treatment algorithms involving multiple treatments have been proposed. These approaches may be counterproductive if poor treatment responses are related to poor adherence. One of the standard recommendations is to have patients use a keratolytic preparation along with a potent topical corticosteroid. Although adding a separate keratolytic agent to the scalp psoriasis treatment regimen may increase the potency of treatment marginally, the increase in complexity of treatment may decrease patient adherence and negatively affect outcome [21,43]. Adherence is typically higher in controlled clinical trials compared to in clinical practice, so that any observed benefits of combination treatments in clinical trials may not carry over to clinical practice. Clinical trial subjects are highly motivated, may be monitored with treatment diaries and medication weights, are seen in regular, closely spaced follow-up visits, and are compensated for participation. These factors boost motivation, provide a greater sense of accountability, and increase treatment adherence compared to clinical practice [10,44,45]. In the clinic setting, a more complex topical regimen may not be used as well as a simple one.

The high efficacy of topical corticosteroid monotherapy observed in clinical trials suggests that a potent topical corticosteroid used alone should also be effective in clinical practice if patients can be effectively encouraged to use the medication regularly. Interventions to improve the efficacy of topical psoriasis therapies in clinical practice would likely benefit from methods to

improve adherence, rather than adding additional therapies and complicating the treatment regimen [21,43]. Choosing among the wide array of vehicles for delivery of topical corticosteroids based on patients' personal preferences is a logical, if not proven, strategy. An early return visit or other physician-patient contact to mimic clinical studies may be valuable as well. If more than one active drug is to be used, using a single product containing a combination of drugs may be advantageous.

Conclusion

High potency topical corticosteroids are usually effective in treating scalp psoriasis in clinical trials. Using a keratolytic agent in conjunction with a topical corticosteroid may provide marginal additional benefit in clinical trials, but that benefit is likely outweighed by the downside of complicating treatment and reducing adherence in the clinical setting, unless a single product containing both medications were used.

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