Dermatology Practical & Conceptual

Tacrolimus in Solution as an Option to Inflammatory Conditions of the Scalp

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ABSTRACT

Introduction: Several dermatological diseases lead to inflammatory conditions of the scalp. Most of these afflictions are recalcitrant and require long term maintenance treatment.

Objectives: We present a case series where topical tacrolimus was used in a solution vehicle for these conditions.

Methods: A total of 22 patients (aged 24-90 years) with confirmed diagnosis of lichen planus pilaris (LPP), discoid lupus (DL), frontal fibrosing alopecia (FFA), erosive pustulosis of the scalp (EPS) or folliculitis decalvans (FD) were evaluated and treated with tacrolimus solution (0.1%) applied twice daily for 1 month, then once daily for another month and alternate days for 4 months. Efficacy was evaluated by an investigator global assessment, clinical and dermoscopic evaluation at weeks 4, 8 and 24. The safety assessment included monitoring of all adverse events.

Results: The study included 13 patients with LPP, 2 with DL, 2 with FD, 2 with EPS and 3 with AFF. After 1 month, 14 patients (63.6%) had a good response and 7 (31.8%) had excellent response. After 2 months, 16 patients (72.7%) had excellent response, and this response was persistent after 6 months of treatment.

Conclusions: Tacrolimus in solution, even if not yet commercially available, was an effective and well tolerated alternative for the maintenance treatment of inflammatory conditions of the scalp.

Introduction

Several dermatological diseases may lead to inflammatory conditions of the scalp. Hyperkeratosis, pruritus, alopecia, and inflammatory signs (such as erythema and purulence) are common symptoms of scalp disorders and therefore a significant overlap in clinical symptomatology can be seen. Most of these afflictions are recalcitrant conditions, and corticosteroids have been widely used, in spite of its well-known side effects of atrophy and rebound [1,2].

Treatment of these conditions varies accordingly to the disease itself, as the pathogenic principles are also different, however, the large amount of hair follicles and intense production of sebum in the region presents a challenge for topical therapies. The most common conditions are lichen planus pilaris (LPP), discoid lupus (DL), frontal fibrosing alopecia (FFA), Erosive pustulosis of the scalp (EPS) and folliculitis decalvans (FD).

Among the drugs that can be used as an alternative to corticosteroids, tacrolimus is a valid option. Tacrolimus is a metabolite of the fungus Streptomyces tsukubaensis, developed as an anti-T-cell immunosuppressor. It acts by inhibiting the production of interleukins, such as IL-2, IL-3, IL-4, TNFα, and GM-CSF, being more effective and with slightly fewer secondary effects than cyclosporine [1]. It is available commercially for oral, intravenous and topical use, being the latter commercialized as creams, ointment or ophthalmologic drops.

Topical immunomodulators (such as tacrolimus and pimecrolimus) have been originally developed for the treatment of atopic dermatitis but their safety profiles and excellent efficacy as anti-inflammatory agents make them attractive candidates to treat many other skin disorders. In this context, these drugs have been extensively studied in dermatology for not only atopic dermatitis but also allergic contact dermatitis, erosive mucosal lichen planus, seborrheic dermatitis, and pyoderma gangrenosum [2].

Objectives

In this article, we discuss the use of tacrolimus in solution, which even if not commercially available can be prepared in a compounding pharmacy, as an alternative for different inflammatory conditions of the scalp that typically require steroids for long-term treatment. We present a case series where it has been used as an alternative for maintenance treatment.

Methods

This study was conducted at a referral Dermatology Unit in Italy, under open-label conditions. Were enrolled patients aged 24–90 years, from both genders (13 females and 9 males), with confirmed histologic diagnosis of LPP, DL, FFA, FD or EPF. Histological diagnosis had been recorded on patients charts, after a 4 mm punch biopsy and analyzed by an experienced dermatopathologist. Patients were informed of the potential benefits and risks of topical application of tacrolimus and had agreed to apply as indicated and signed the informed consent. Patients who did not complete the 24-week follow-up were excluded from the study.

Assessment included the patients age, gender, clinical and dermoscopical images, past therapies and adverse events. All patients after enrolment were subsequently followed-up and assessed by the same 3 dermatologists at 4-week intervals until 24 weeks, and related data and information regarding improvement were recorded. An Investigator Global Assessment (IGA) score of poor, good or excellent response was stablished in every visit.

The response rate was graded as excellent (>75% of hair regrowth or absence of inflammatory signs), good (>50 to 75% of hair regrowth or improve of inflammatory signs), poor (>0 to 25%), and no response. The effective rate = (good + excellent cases number)/total cases number) was calculated. Additionally, local adverse reactions, including erythema, atrophy, telangiectasia, pigment changes, and folliculitis were observed throughout the study period.

Tacrolimus solution 0.1% (Tacrolimus Monohydrate 0.5-mg/mL in SyrSpend™ SF solution, pH 4, Fagron) was prepared by the same pharmacist, as it is not commercially available, and was applied twice daily for one month, then once daily for another month and alternate days for 4 months. Safety parameters included symptoms and objective findings. Patients were required not to apply other medications during the study period.

Results

Baseline demographics of the 22 patients enrolled were recorded, including 13 women and 9 men, with ages ranging from 24 to 90 years. Of these 22, 13 patients had a diagnosis of LPP, 2 of DL, 2 of FD, 2 of EPS and 3 of FFA, all with previous punch biopsies that confirmed histologically the diagnosis. The average course of disease was of 8 ± 3 months.

The overall effective rate, defined as some degree of hair regrowth and cessation of inflammation (good or excellent response), was of 95,4% and 86% after 1 and 6 months respectively.

Table 1 presents the results for each condition.

Mild redness and scratch occurred in one patient. No serious local adverse reactions were detected. One patient with LPP did not respond to the therapy and two patients with LPP lost response after 6 months of therapy.

Figures 1-4 show clinical and tricoscopic results before and after treatment.

Table 1. Results

AGE	GENDER	DIAGNOSIS	IGA 1 Month	IGA 2 Months	IGA 6 Months
62	Female	LPP	2	3	3
24	Male	LPP	3	2	1
52	Male	LPP	2	2	1
75	Female	LPP	2	2	2
72	Female	LPP	2	3	3
73	Female	LPP	2	2	3
63	Female	LPP	2	3	3
36	Male	LPP	2	3	2
61	Male	LPP	0	0	0
40	Female	LPP	3	3	3
70	Female	LPP	2	3	3
54	Female	LPP	2	3	3
51	Female	LPP	3	3	2
90	Male	EPS	3	2	2
84	Male	EPS	2	3	3
77	Female	DL	2	3	2
74	Male	DL	3	3	3
40	Male	FD	3	3	3
53	Male	FD	2	3	3
62	Female	FFA	2	3	3
64	Female	FFA	2	2	2
47	Female	FFA	3	3	3

IGA: Investigators Global Assessment (1: poor / 2: good / 3: excellent); LPP: Lichen Planus Pilaris, FD: Folliculitis Decalvans; EPS: Erosive Pustulosis of the Scalp; DL: Dyscoid Lupus; FFA: Fibrosing Frontal Alopecia

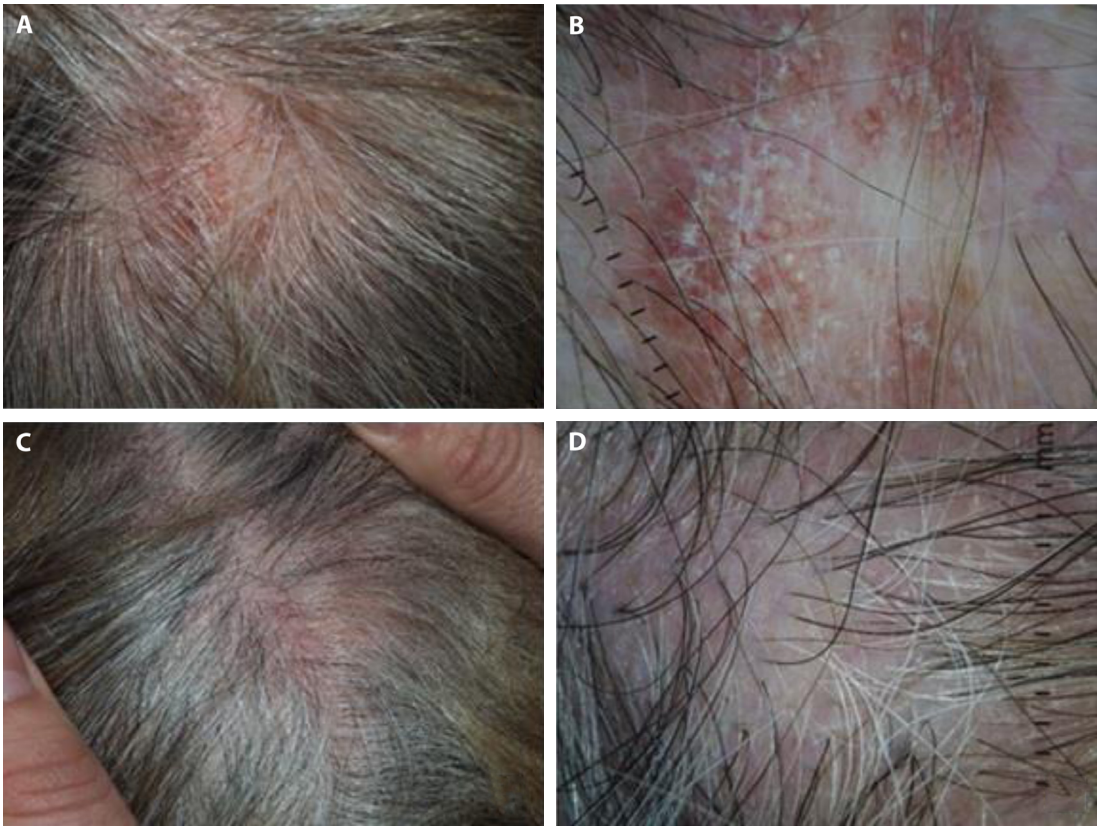

Figure 1. (A) Clinical presentation at first visit of a 68-year-old female with dyscoid lupus. An erythematous and desquamative plaque of the vertex. (B) Trichoscopy (20x) showing squamation, prominent arborizing blood vessels and brown scattered pigmentation. (C) Clinical presentation after 1 month of treatment. (D) Trichoscopy showing no more signs of inflammation.

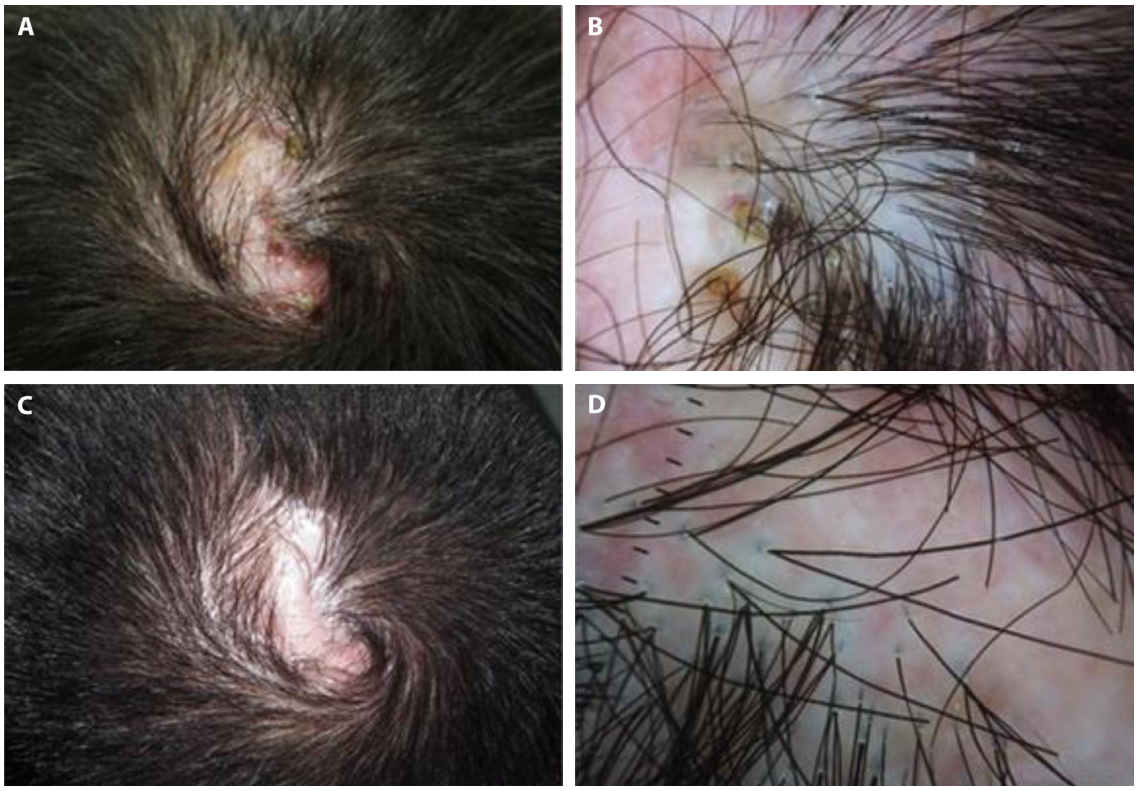

Figure 2. (A) Clinical image of a scarring alopecia of the vertex with signs of inflammation, histologically compatible with folliculitis decalvans. (B) Trichoscopy showing follicular hyperkeratosis, perifollicular erythema, tufted hairs, and cicatricial white patches. (C) Clinical image of a scarring alopecia of the vertex without signs of inflammatory activity. (D) Trichoscopy of a scarring alopecia.

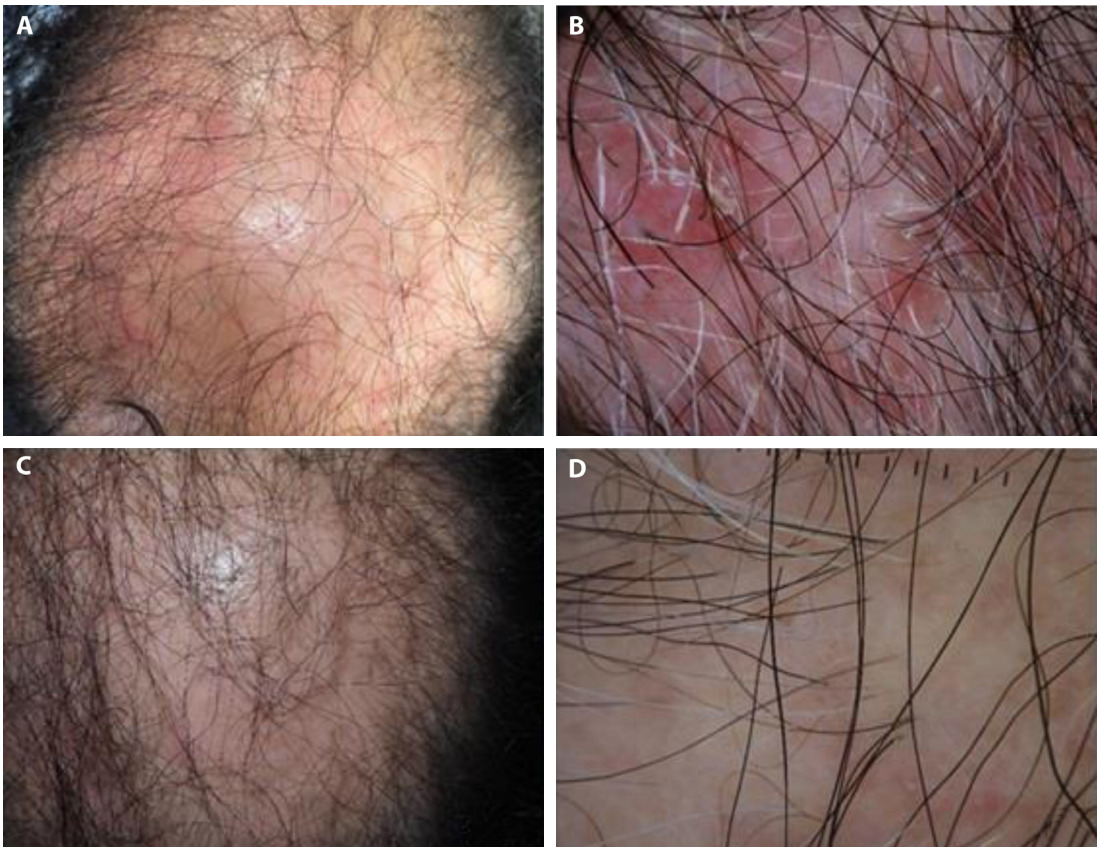

Figure 3. (A) Clinical image of a scarring alopecia of the vertex with signs of desquamation, histologically compatible with lichen planus pilaris. (B) Trichoscopy reveals absent follicles, white dots, tubular perifollicular scale and perifollicular erythema, follicular inflammation and fibrosis. (C) Clinical image of a scarring alopecia of the vertex without signs of inflammatory activity. (D) Trichoscopy of a spent scarring alopecia.

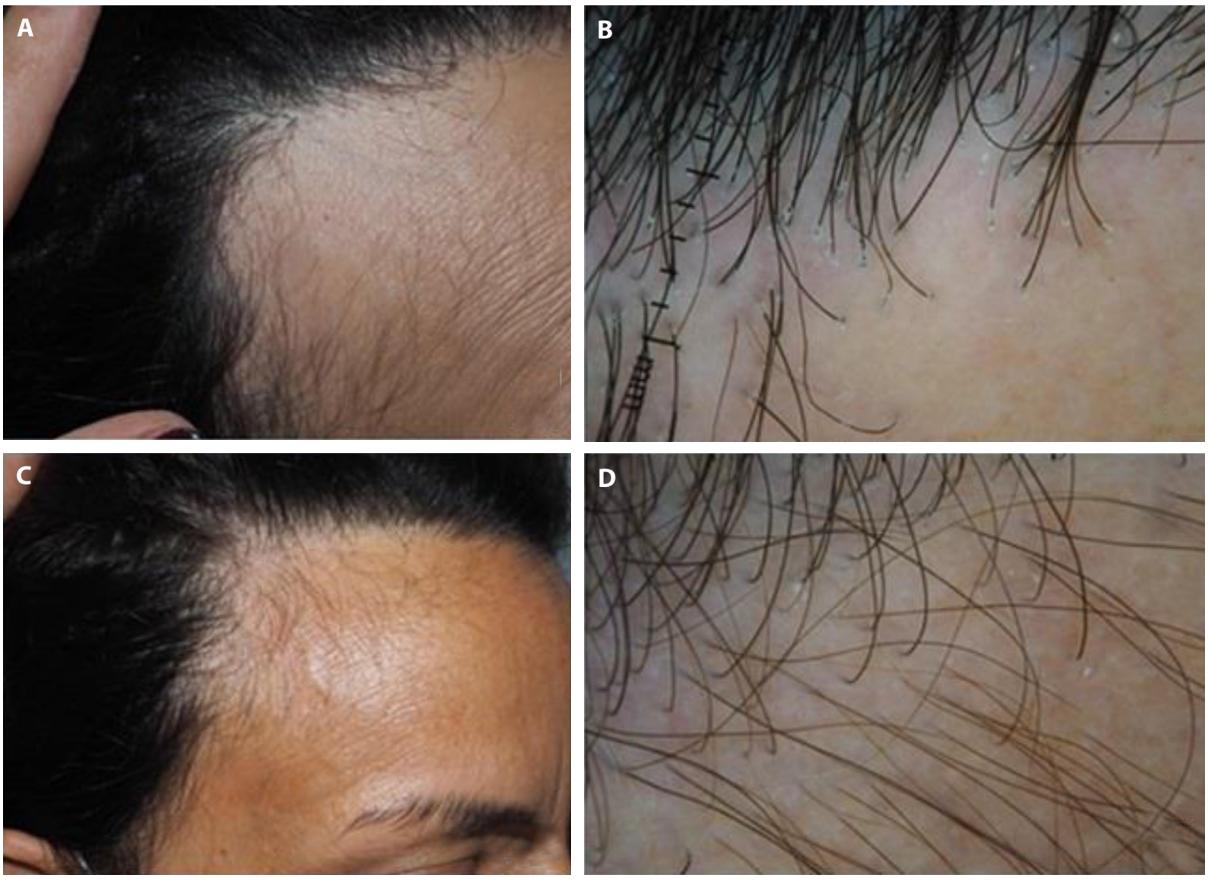

Figure 4. (A) Clinical image of a scarring frontotemporal alopecia histologically compatible with frontal fibrosing alopecia. (B) Trichoscopy showing follicular hyperkeratosis, perifollicular erythema, lonely hair and cicatricial white patches. (C) Clinical image of repilation after 6 months without signs of inflammatory activity. (D) Trichoscopy revealing discreet follicular hyperkeratosis and repilation.

Conclusions

In this case series we discussed the use of tacrolimus in a solution for different inflammatory conditions of the scalp. Even if those conditions differ in pathology and have different approaches regarding therapy, topical steroids are usually the first line of therapy for LP, DL, FFA and EPS and antibiotics for FD. Sometimes, however, corticosteroids might not be completely effective and these conditions when left untreated might evolve into scarring alopecia. Literature review did not show any results for the use of tacrolimus in solution instead of ointment or cream as an alternative treatment for inflammatory conditions of the scalp [10-18].

The majority of studies available consider the treatment of LP and DL as the same regarding all anatomic sites, except for oral mucosa, being the use of topical or systemic corticosteroids the first line therapy [10,11]. However, most patients eventually relapsed, since the corticosteroid treatment could not be maintained for longer periods.

FFA has been extensively studied in the more recent years, and current consensus recommends topical treatments including corticosteroids, minoxidil, and calcineurin inhibitors and/or systemic treatments including 5α-reductase inhibitors, hydroxychloroquine, and retinoids [13]. Intralesional triamcinolone acetonide has also been described, with different response rates and recurrence levels.

FD, even though several publications are available regarding the treatment, most studies evaluated had small sample size, lacked control groups, and randomization, and in these studies combination of clindamycin and rifampicin were the most commonly referred [14]. Nevertheless, we agree initial treatment with antibiotics is required, most patients recur after the treatment, so maintenance with tacrolimus solution is a viable option. A study that evaluated 4 patients with FD with tacrolimus in ointment showed that these patients significantly controlled their condition, stopping inflammatory lesions and progression of the disease, although alopecia and tufted hairs remained unchanged and the discontinuation of the therapy produced rapid relapses in all cases [19].

Calcineurin inhibitors have already been described in the literature as a good choice for inflammatory conditions of the scalp. Some case reports showed only limited improvement in LPP (total number of patients: 12; global response rate: 23.1% (2 of 12); response rate in monotherapy: 11.1%) [15]. Regarding EPS, tacrolimus has recovered skin atrophy both during and after treatment and also led to 40–50% regrowth of hair after 2 months of therapy [16].

One randomized double-blind study of 38 individuals, 14 with DLE, found significant improvement in those treated with 0.1% tacrolimus ointment applied twice daily for 3 months compared to vehicle [17].

In a study on 92 patients with FFA, patients treated with 0.3% tacrolimus were significantly more likely to stabilize in 3 months compared with patients treated with clobetasol/betamethasone (P 0.0297), but with longer median time of stabilization [18].

These studies current limitation are small simple size and the lack of comparison between regular treatment with tacrolimus in cream/ointment, because most patients did not comply on applying the cream on the scalp, making the comparison of outmost difficulty. On our study, a good compliance was observed and most patients had a satisfactory response for their conditions. Limitation of this study is that, as a case series, it does not have a control group, and further studies should address individually each condition in a controlled trial. Still, tacrolimus as solution remained a viable option particularly for a long-term maintenance treatment.

Our case series showed tacrolimus as solution could be an interesting alternative, as it is not related to atrophy if used for long periods and therefore can be of great use for inflammatory conditions that are usually prone to recurrences. Moreover, this vehicle is more comfortable for patients on the scalp than ointment, especially female patients where the cosmetic aspect of the hair is usually taken into consideration when complying with a therapy. Further long-term comparative studies are required for better understanding.

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