ORIGINAL REPORT

Systemic Treatments for Lichen Planopilaris and Frontal Fibrosing Alopecia: A Retrospective Study of 315 Patients

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Lichen planopilaris and frontal fibrosing alopecia are common variants of primary lymphocytic cicatricial alopecia, leading to permanent hair loss. Despite widespread use of various systemic treatments, evidence-based guidelines for these conditions are lacking. This study investigates the effectiveness of systemic treatment options in patients with lichen planopilaris and frontal fibrosing alopecia through a retrospective cohort analysis. Medical records of patients treated at the Department of Dermatology between 2016 and 2022 at the Erasmus University Medical Center Rotterdam, the Netherlands were reviewed. Of 315 patients identified (161 lichen planopilaris and 154 frontal fibrosing alopecia), the majority were female (90.5%), with hydroxychloroquine being the most common systemic treatment, used by 65.2% of lichen planopilaris and 57.8% of frontal fibrosing alopecia patients. Methotrexate had the highest response rate for lichen planopilaris (79.2%), while retinoids showed the highest response for frontal fibrosing alopecia (73.9%). However, treatments with cyclosporine A and retinoids had higher discontinuation rates due to side effects. This study suggests methotrexate and cyclosporine A may be most effective for lichen planopilaris, and cyclosporine A and retinoids for frontal fibrosing alopecia, though side effects remain a concern. Limitations include the retrospective design and the absence of standardized outcomes. Prospective studies are recommended to validate these findings.

Key words: cicatricial alopecia; lichen planopilaris; frontal fibrosing alopecia; inflammatory hair disorder; hair loss; systemic treatment

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SIGNIFICANCE

Lichen planopilaris and frontal fibrosing alopecia are chronic, scarring hair disorders causing permanent hair loss and significantly impacting quality of life. This study identifies methotrexate and cyclosporine A as effective treatments for lichen planopilaris and highlights retinoids and cyclosporine A for frontal fibrosing alopecia. These findings provide valuable insights into treatment selection, helping clinicians make evidence-based decisions to improve outcomes for patients with these debilitating conditions. Future prospective studies are necessary to refine and standardize therapeutic strategies.

Cicatricial alopecia encompasses a group of rare chronic inflammatory hair disorders resulting in irreversible hair loss. Cicatricial alopecia can be primary, with the hair follicle itself as a target of inflammation, or secondary, with hair follicle destruction due to a non-follicle-directed cause (1–3). Lichen planopilaris (LPP) and frontal fibrosing alopecia (FFA) are the most common forms of primary lymphocytic cicatricial alopecia (4–6). LPP usually presents with patchy or diffuse alopecic patches, most frequently at the vertex or parietal scalp (7–9). FFA is characterized by selective involvement of the frontotemporal band resulting in a receding hairline, is commonly associated with eyebrow alopecia, and usually affects postmenopausal women (8, 10, 11). Subjective symptoms in the areas of active disease include pruritus, burning sensation, and trichodynia (6, 7).

The pathogenesis of LPP and FFA remains largely unclear, but there are several hypotheses. However, the most widely accepted hypothesis suggests a T-cell mediated autoimmune response to an unknown antigen leading to destruction of follicular stem cells in the bulge region of the hair follicle (1, 5, 7). The hair follicle thereby loses its potential to regrow, resulting in cicatricial alopecia. In addition, pilosebaceous dysfunction leading to follicular inflammation is believed to have involvement in pathogenesis (12–14). Despite sharing common pathways, LPP and FFA diverge at some point. LPP and FFA are microscopically very similar diseases but can exhibit distinct clinical phenotypes.

Currently, the only realistic treatment goal in managing LPP and FFA is to stop disease progression, and reduce symptoms. Evaluating treatment options for LPP and FFA is challenging due to limited literature and the lack of randomized controlled trials. Because (inter) national therapeutic protocols and standardized outcome measures are missing, treatment is largely empirical and mostly based on expert opinion. Topical corticoste-

roids, intralesional triamcinolone acetonide injections, and topical minoxidil are commonly used as first-line therapy (1). Systemic treatment options for LPP that have been reported include hydroxychloroquine (HCQ), methotrexate (MTX), oral corticosteroids, cyclosporine A (CsA), pioglitazone, doxycycline, mycophenolate mofetil/mycophenolic acid (MMF/MPA), JAK inhibitors, and retinoids (6–8). Treatment for FFA resembles that of LPP. However, there have been reports of disease stabilization in FFA patients using 5-alpha-reductase inhibitors and topical calcineurin inhibitors (1, 15). Given the significant impact on the quality of life and mental health of patients, more evidence on the effectiveness and adverse effects of current treatments is needed and could improve treatment response and therefore improve the quality of life of these patients (16). Therefore, the aim of this study was to investigate the effectiveness of currently used systemic therapies for treatment of LPP and FFA.

MATERIALS AND METHODS

Study design

A retrospective observational cohort study was performed using medical records of patients diagnosed with LPP or FFA, at the Department of Dermatology and Venereology, Erasmus MC University Medical Center in Rotterdam, the Netherlands.

Study population and data collection

All patients diagnosed with International Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) diagnosis: L66 cicatricial alopecia, between July 2016 and July 2022, from the Department of Dermatology, Erasmus MC University Medical Center, were included. Data were collected from the patients' electronic medical records. This study was approved by the Institutional Review Board (IRB), reference number (MEC-2022-0679). The inclusion criteria consisted of a diagnosis of LPP or FFA based on clinical presentation, with histopathological confirmation if necessary, in patients aged 18 years or older. Histopathological confirmation was performed only when clinically indicated. LPP and FFA often present as distinct clinical entities, and in many cases histological confirmation was deemed unnecessary by the treating physicians or declined by the patients. Patients with other forms of cicatricial alopecia, including folliculitis decalvans and dissecting cellulitis of the scalp, were excluded from this study. Patients with overlapping clinical features of both LPP and FFA were also excluded to ensure diagnostic specificity. Furthermore, individuals with only a single recorded visit were excluded, as their treatment response could not be adequately assessed.

Demographic and clinical data were collected from medical records, including disease features at the first and last visit, such as disease type, localization, affected area, disease duration, histopathological and trichoscopic findings, and Numeric Rating Scale (NRS) scores for the burden of disease, pain, and itch. Furthermore, types of different treatment options were reported; first-line treatment options (topical corticosteroids, topical calcineurin inhibitors, intralesional corticosteroids, minoxidil, and tetracyclines). Response to treatment, duration of treatment, and reason for discontinuation of systemic treatment options (HCQ, MTX, CsA, retinoids, MMF/MPA, and pioglitazone) were evaluated. Clinical pictures, if available, were used to verify the localization, affected area, and trichoscopic activity.

Assessment of treatment response

The primary outcome of this study was treatment response in patients using systemic medication. The effect of treatment was determined by integrating symptoms, trichoscopic findings, and size of the affected area. Treatment response was divided into 3 groups. No response was defined as progression of symptoms (itch and pain), hair loss, and trichoscopic activity. Moderate response was defined as the improvement of reported symptoms, less hair loss progression, or reduction in trichoscopic activity. Good response was defined as the absence of symptoms, no further hair loss, and no trichoscopic activity.

Trichoscopic activity was classified as: no activity, moderate activity, and severe activity. No activity was defined as absence of perifollicular erythema and follicular hyperkeratosis. Moderate activity was defined as perifollicular erythema or follicular hyperkeratosis. Severe activity was defined as perifollicular erythema and follicular hyperkeratosis and induration. The affected area was categorized into 3 groups: small, moderate, and large. In patients with LPP, small was defined as $< 25cm^2$, moderate as $25cm^2$–$100cm^2$, and large as $> 100cm^2$ or multiple lesions. In patients with FFA, small was defined as recession of the frontal hairline, moderate as recession of the frontal and temporal hairlines, and large as recession of the frontal, temporal, and occipital hairlines. Worsening, stable, and improving were used to describe changes in trichoscopic activity, while regression, stable, and progression were used to assess changes in the affected area. For example, worsening in trichoscopic activity was defined as an increase in severity (e.g., from none to moderate or severe), whereas progression in the affected area referred to an increase in hair loss extent (e.g., from small to moderate or large).

Statistical analysis

Statistical analysis was performed using SPSS version 28.0.1.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics were computed by type and summarized the baseline characteristics. Variables were first examined for normality

of distributions by Shapiro–Wilk tests. Numeric variables were reported with frequency and percentage, and categorical variables were illustrated by mean and standard deviation. *T*-tests were used to compare the differences between groups. The treatment response was calculated per treatment option, and χ^2 tests were used to compare different subgroups. Missing values were excluded from the analysis; only valid percentages were shown. *P*-values < 0.05 were considered significant.

RESULTS

Study cohort

A total of 562 patients with the ICD-10 diagnosis cicatricial alopecia were included, of which 315 patients met the inclusion criteria. This included 161 LPP patients and 154 FFA patients (**Fig. 1**). In total, 247 patients with other forms of cicatricial alopecia ($n = 218$), a combination of LPP and FFA ($n = 24$), or age at diagnosis below 18 years ($n = 5$) were excluded.

Patient characteristics

Demographic and clinical characteristics of patients in both groups are summarized in **Table I**. Significant differences were observed in sex and age of onset between the LPP and FFA groups, with 82.6% of LPP patients being female and a median age of onset at 49 years, compared with 98.7% of female FFA patients with a median age of onset at 57 years ($p < 0.001$). The median follow-up was 17 months. Most patients had Fitzpatrick skin type II (60.1%).

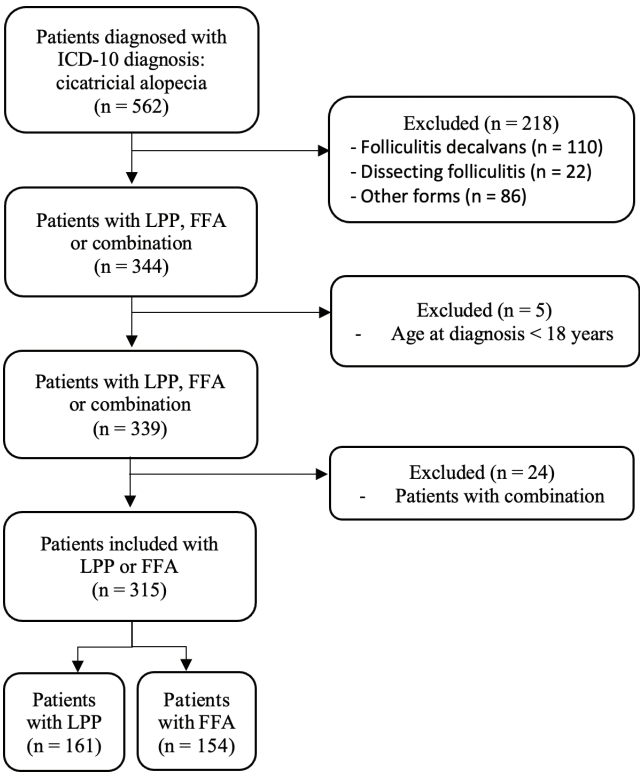

Fig. 1. Flowchart of study population.

Clinical features

The distribution of lesions varied between LPP and FFA, with frontal and temporal involvement being more prevalent in FFA than in LPP. In contrast, parietal and occipital involvement was noted more frequently in LPP than in FFA (Table I). Eyebrow involvement occurred more often in FFA patients than in LPP patients (65.6% vs 11.8%; $p < 0.001$).

Increased trichoscopic activity between first and last visit was observed more frequently in FFA patients (5.4%) compared with LPP patients (0.7%), and decreased trichoscopic activity was observed more frequently in LPP patients (29.6%) than in FFA patients (23.8%) ($p = 0.036$). An increase in the size of the affected area was seen more often In LPP patients compared with FFA patients, 15.5% vs 5.5% respectively ($p = 0.020$). An overview of trichoscopic activity and affected area is provided in Table SI. The mean burden of disease NRS score (0–10) in LPP patients was 7.4 at first visit and 7.2 last visit, and in FFA patients 7.0 at first visit and 7.7 at last visit.

Treatment options

The majority of patients received topical corticosteroids (LPP 93.2%; FFA 90.9%; **Table II**), mostly in combination with other treatments. There was no significant difference in the percentage of patients who were treated with intralesional corticosteroid injections between LPP and FFA (25.5% vs 29.2%). Topical minoxidil was used more frequently in FFA patients compared with LPP patients (54.4% vs 26.1%; $p < 0.001$), as well as topical calcineurin inhibitors (34.4% vs 22.4%; $p = 0.018$). Tetracyclines were used more often in LPP patients than FFA patients (25.5% vs 6.5%; $p < 0.001$). In both groups, HCQ was the most frequently used systemic treatment (LPP: 65.2%, FFA: 57.8%). The most commonly used dose for HCQ was 200 mg twice daily. Among LPP patients, 39.8% received MTX, 20.5% CsA, and 13.0% retinoids. The most frequently used dose for MTX was 15 mg per week, for CsA it was 3–5 mg/kg/day, and for retinoids, specifically isotretinoin, it was 20 mg per day. Among FFA patients, MTX was administered to 24.0%, retinoids to 18.2%, and CsA to 11.7% of the patients. The statistical analysis excluded the patients treated with MMF/MPA and pioglitazone due to their small sample size.

Systemic treatment response

Table III and **Fig. 2** summarize the responses to the different systemic treatment options. The use of 2 or more concomitant systemic treatments was not considered in this table.

Table I. Patient characteristics and clinical features

Factor	Lichen planopilaris (*n* = 161)	Frontal fibrosing alopecia (*n* = 154)	Total (*n* = 315)	*p*-value
Sex, female, *n* (%)	133 (82.6%)	152 (98.7%)	285 (90.5%)	< 0.001[a]
Fitzpatrick skin phototype, *n* (%)				
I	11 (6.8%)	13 (8.6%)	24 (7.7%)	0.005[a]
II	84 (52.2%)	104 (68.4%)	188 (60.1%)	
III	19 (11.8%)	7 (4.6%)	26 (8.3%)	
IV	12 (7.5%)	13 (8.6%)	25 (8.0%)	
V	20 (12.4%)	11 (7.2%)	31 (9.9%)	
VI	15 (9.3%)	4 (2.6%)	19 (6.1%)	
Age of onset (years), median (IQR)	49.0 (21.0)	57.0 (14.0)	52.0 (20.0)	< 0.001[b]
Localization[c], n (%)				
Frontal	54 (34.2%)	152 (99.3%)	206 (66.2%)	< 0.001[a]
Temporal	27 (17.1%)	87 (56.9%)	114 (36.7%)	< 0.001[a]
Parietal	144 (91.1%)	6 (3.9%)	150 (48.2%)	< 0.001[a]
Occipital	44 (27.8%)	22 (14.4%)	66 (21.2%)	0.004[a]
Eyebrow involvement, n (%)	19 (11.8%)	101 (65.6%)	120 (38.1)	< 0.001[a]
Histopathology, *n* (%)				
No biopsies	42 (26.1%)	99 (64.3%)	141 (44.8%)	< 0.001[a]
No histopathological confirmation	40 (24.8%)	14 (9.1%)	54 (17.1%)	
Histopathological confirmation	79 (49.1%)	41 (26.6%)	120 (38.0%)	
Follow-up[d] (months), median (IQR)	15.0 (33.0)	17.0 (27.0)	17.0 (30.0)	0.242[b]
Trichoscopic activity, *n* (%)				
Worsening	1 (0.7%)	8 (5.4%)	9 (3.0%)	0.036[a]
Stable	106 (69.7%)	104 (70.7%)	210 (70.2%)	
Improving	45 (29.6%)	35 (23.8%)	80 (26.8%)	
Affected area (spreading), *n* (%)				
Regression	1 (0.7%)	1 (0.7%)	2 (0.7%)	0.020[a]
Stable	124 (83.8%)	136 (93.8%)	260 (88.7%)	
Progression	23 (15.5%)	8 (5.5%)	31 (10.6%)	
Perifollicular erythema, *n* (%)				
First visit	107 (68.2%)	100 (68.0%)	207 (68.1%)	0.981[a]
Last visit	81 (54.4%)	84 (57.9%)	165 (56.1%)	0.538[a]
Perifollicular hyperkeratosis, *n* (%)				
First visit	125 (80.6%)	103 (71.5%)	228 (76.3%)	0.064[a]
Last visit	84 (57.1%)	81 (56.3%)	165 (56.7%)	0.878[a]
Numeric Rating Scale first visit, mean (SD)				
Burden of disease	7.4 (2.2)	7.0 (2.4)	7.2 (2.3)	0.341[b]
Pain	1.0 (2.4)	0.3 (1.4)	0.6 (1.9)	0.009[b]
Itch	2.6 (3.4)	1.0 (2.3)	1.7 (3.0)	< 0.001[b]
Numeric Rating Scale last visit, mean (SD)				
Burden of disease	7.2 (2.7)	7.7 (2.4)	7.5 (2.5)	0.538[b]
Pain	0.4 (1.4)	0.2 (1.0)	0.3 (1.2)	0.191[b]
Itch	1.3 (2.6)	0.5 (1.8)	0.9 (2.3)	0.018[b]

Valid percentages are shown. [a]χ^2 test. [b]Mann–Whitney *U* test. [c]Total may add up to > 100% due to multiple site involvement. [d]Patients with single visit were excluded.

For LPP, HCQ was the most frequently used (65.2%, 105/161 patients) systemic medication, resulting in 30.8% moderate responses and 12.5% good responses. MTX demonstrated the highest response rates, with 32.8% achieving moderate responses and 32.8% achieving good responses. CsA showed 21.2% moderate responses and 27.3% good responses in LPP. Retinoids showed the lowest response rates in LPP, with 40.0% showing no response and only 5.0% achieving a good response.

Table II. Treatment options

Type of treatment, *n* (%)	LPP (*n* = 161)	FFA (*n* = 154)	*p*-value
Topical corticosteroids	150 (93.2%)	140 (90.9%)	0.459
Topical calcineurin inhibitors	36 (22.4%)	53 (34.4%)	0.018
Intralesional corticosteroids	41 (25.5%)	45 (29.2%)	0.455
Topical minoxidil	42 (26.1%)	84 (54.4%)	< 0.001
Tetracyclines	41 (25.5%)	10 (6.5%)	< 0.001
Hydroxychloroquine	105 (65.2%)	89 (57.8%)	0.176
Methotrexate	64 (39.8%)	37 (24.0%)	0.003
Ciclosporin	33 (20.5%)	18 (11.7%)	0.034
Retinoids	21 (13.0%)	28 (18.2%)	0.208
Mycophenolate mofetil	7 (4.3%)	–	–
Pioglitazone	3 (1.9%)	3 (1.9%)	0.956

LPP: lichen planopilaris; FFA: frontal fibrosing alopecia.

For FFA, HCQ was also the most frequently used systemic treatment (89 of 154, 57.8%), resulting in 38.2% moderate responses, and 12.4% good responses. Retinoids showed 39.3% moderate responses and 21.4% good responses. MTX and CsA demonstrated similar outcomes, with 21.6% and 22.2% moderate responses and 27.0% and 27.8% good responses, respectively.

Responders vs non-responders

Considering the group of moderate and good response as responders and the no-response group as non-responders, these results are represented in **Table IV**. The largest group of responders in LPP patients were treated with MTX (79.2% responders vs 20.8% non-responders). CsA had the second largest percentage of responders (69.6% responders vs 30.4% non-responders), followed by HCQ (53.6% responders vs 46.4% non-responders), and the smallest percentage of responders belonged to retinoids (38.5% responders vs 61.5% non-responders). The percentage of responders in FFA patients was the highest in the retinoids group (73.9% responders vs 26.1% non-

Table III. Systemic treatment responses

	Lichen planopilaris		Frontal fibrosing alopecia	
Systemic treatment	*n*, (%)	Duration[a] (months), median (IQR)	*n*, (%)	Duration[a] (months), median (IQR)
Hydroxychloroquine	105 (65.2%)	9.0 (18)	89 (57.8%)	12.0 (23)
No response	39 (37.5%)	7.0 (9)	31 (34.8%)	9.0 (8)
Moderate response	32 (30.8%)	19.5 (32)	34 (38.2%)	23.0 (35)
Good response	13 (12.5%)	23.0 (41)	11 (12.4%)	24.0 (17)
Unknown	20 (19.2%)	2.5 (3)	13 (14.6%)	3.5 (4)
Methotrexate	64 (39.8%)	7.0 (11)	37 (24.0%)	8.0 (13)
No response	11 (17.2%)	7.0 (9)	13 (35.1%)	8.0 (8)
Moderate response	21 (32.8%)	7.0 (9)	8 (21.6%)	7.5 (4)
Good response	21 (32.8%)	11.0 (10)	10 (27.0%)	26.5 (30)
Unknown	11 (17.2%)	2.0 (2)	6 (16.2%)	1.0 (–)
Ciclosporin	33 (20.5%)	9.0 (11)	18 (11.7%)	5.0 (13)
No response	7 (21.2%)	2.0 (8)	5 (27.8%)	5.0 (5)
Moderate response	7 (21.2%)	14.0 (19)	4 (22.2%)	6.5 (14)
Good response	9 (27.3%)	12.0 (12)	5 (27.8%)	20.0 (31)
Unknown	10 (30.3%)	5.0 (–)	4 (22.2%)	1.5 (–)
Retinoids	21 (13.0%)	5.0 (2)	28 (18.2%)	8.5 (8)
No response	8 (40.0%)	4.5 (3)	6 (21.4%)	5.0 (2)
Moderate response	4 (20.0%)	6.0 (15)	11 (39.3%)	10.5 (13)
Good response	1 (5.0%)	–	6 (21.4%)	10.0 (7)
Unknown	7 (35.0%)	5.0 (4)	5 (17.9%)	4.0 (12)

[a]Treatment durations < 1 month were excluded.

responders); the second largest percentage of responders belonged to the CsA group (64.3% responders vs 35.7% non-responders), followed by HCQ (59.2% responders vs 40.8% non-responders), and MTX (58.1% responders vs 41.9% non-responders).

Reasons for discontinuation of systemic treatment

The reasons for treatment discontinuation varied between the different systemics (**Table V**). HCQ was most frequently discontinued because of insufficient treatment effect (LPP 53.0%, FFA 63.3%). In addition, a substantial percentage of patients discontinued HCQ because of side effects (LPP 31.8%, FFA 20.4%). In the MTX group, similar results were observed as in the HCQ group, with most cases for discontinuation due to insufficient effect (LPP 51.6%, FFA 62.5%). In the CsA group, the number of patients who discontinued because of side effects was higher (LPP 80.0%, FFA 41.2%) than in the HCQ and MTX groups. In the retinoids group, similar results were seen to those in the CsA group, with the majority of patients discontinuing due to side effects (LPP 62.5%, FFA 64.3%). No major side effects were reported in our cohort.

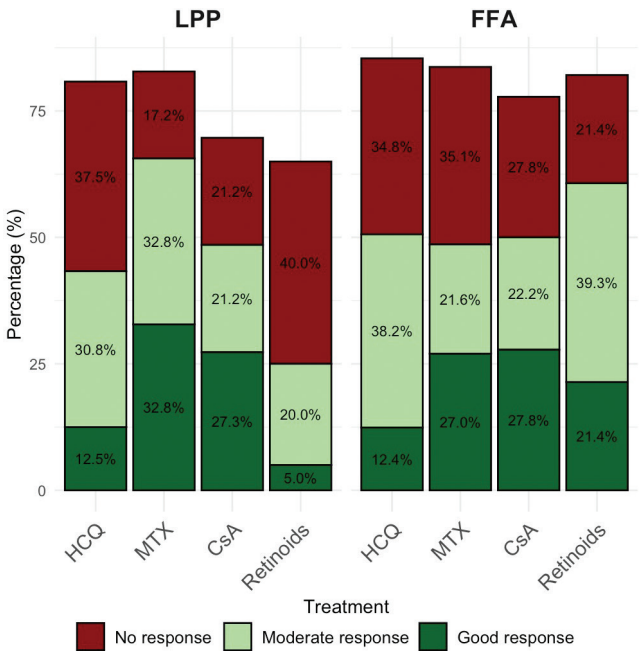

Fig. 2. Systemic treatment responses.

DISCUSSION

Currently, there are no evidence-based treatment protocols for LPP and FFA. Therefore, we investigated the effectiveness of systemic treatment options used among LPP and FFA patients in our hospital. This is one of the largest studies investigating LPP and FFA treatment to date. It is also the first study to analyse demographic, clinical, and treatment features of LPP and FFA patients in the Netherlands. LPP and FFA are currently considered to be separate entities, with a common initial pathway (8, 10, 17); therefore we analysed and compared them with each other. We found that LPP patients most frequently used HCQ, followed by MTX, CsA, and retinoids. These findings align with previous publications (7, 18, 19), confirming the current trends in treatment choices. In LPP patients, MTX was found to show the best treatment response. Furthermore, CsA is another effective therapeutic option with good response rates, and these results are in accordance with previous studies (6, 20, 21). HCQ gave poorer response rates than MTX and CsA; nevertheless, HCQ was superior to retinoids. HCQ is most frequently prescribed due to its ease of use and established safety profile. However, our findings indicate that MTX demonstrated the highest effectiveness in LPP patients,

Table IV. Responders vs non-responders

	Lichen planopilaris		Frontal fibrosing alopecia		
Systemic treatment	*n* (%)	Duration (months), median (IQR)	*n* (%)	Duration (months), median (IQR)	*p*-value
Hydroxychloroquine	84		76		0.473[a]
Non-responders	39 (46.4%)	7.0 (9)	31 (40.8%)	9.0 (8)	0.004[b]
Responders	45 (53.6%)	20.0 (38)	45 (59.2%)	24.0 (32)	0.001[c]
Methotrexate	53		31		0.038[a]
Non-responders	11 (20.8%)	7.0 (9)	13 (41.9%)	8.0 (8)	0.952[b]
Responders	42 (79.2%)	8.0 (11)	18 (58.1%)	8.5 (25)	0.073[c]
Ciclosporin	23		14		0.739[a]
Non-responders	7 (30.4%)	2.0 (8)	5 (35.7%)	5.0 (5)	0.011[b]
Responders	16 (69.6%)	12.0 (17)	9 (64.3%)	11.0 (19)	0.227[c]
Retinoids	13		23		0.036[a]
Non-responders	8 (61.5%)	4.0 (1)	6 (26.1%)	5.0 (2)	0.323[b]
Responders	5 (38.5%)	6.0 (10)	17 (73.9%)	10.5 (9)	0.073[c]

Note: Valid percentages are shown. Unknown responses were excluded. Treatment durations < 1 month were excluded.
[a]Pearson χ^2 test for number of LPP patients vs FFA patients in systemic treatment group. [b]ANOVA test for duration of responders vs non-responders in LPP group. [c]ANOVA test for duration of responders vs non-responders in FFA group.

suggesting it should be considered earlier in the treatment algorithm. Adjusting treatment protocols to prioritize MTX could potentially improve patient outcomes.

Our study showed that FFA patients were most frequently treated with HCQ, followed by MTX, retinoids, and CsA. Notably, patients in the retinoids group had the highest overall response rate (moderate and good responses), while the CsA group had the highest proportion of good responses. This finding offers a new perspective on FFA treatment, as previous literature (6, 15, 22–24) has primarily focused on HCQ and 5-alpha-reductase inhibitors. The promising results with retinoids and CsA suggest they may be more effective options than previously considered, warranting further investigation. However, a direct comparison with 5-alpha-reductase inhibitors was not possible due to the limited number of patients using these drugs in our cohort.

Furthermore, our study has several limitations that need to be considered. This study was conducted using a retrospective design, resulting in a relatively high amount of missing data, including the lack of histopathological confirmation in certain cases, which could influence diagnostic accuracy, as histopathology was performed only when deemed necessary by the treating physicians. Additionally, the absence of standardized outcome measures to determine disease severity and score the treatment response posed a limitation. Two scoring systems have been published to scale the severity of disease, the LPP Activity Index (LPPAI) by Chiang et al. (25), in 2010, and the FFA Severity Index (FFASI) by Holmes et al. (26), in 2016. Considering the retrospective character of our study, the LPPAI and FFASI could not be applied. Nonetheless, we assessed and scaled the disease severity and treatment response using data extracted from medical records, with documented photographs. Documented photographs were reviewed by 1 researcher to avoid variation in interpretation; in case of doubt there was deliberation with co-researchers. A third limitation is the difficulty in attributing the treatment effect to a specific therapy as various combinations of topical and systemic treatments were commonly used. Therefore, the treatment response could be attributed to another therapy or the combination of multiple simultaneous therapies.

Table V. Reasons for discontinuation

Discontinuation due to	Lichen planopilaris *n* (%)	Frontal fibrosing alopecia *n* (%)
Hydroxychloroquine	66/105 (62.9%)[a]	49/89 (55.0%)[a]
Sufficient effect	10 (15.2%)	8 (16.3%)
Insufficient effect	35 (53.0%)	31 (63.3%)
Side effects	21 (31.8%)	10 (20.4%)
Methotrexate	31/64 (48.4%)[a]	24/37 (64.9%)[a]
Sufficient effect	3 (9.7%)	3 (12.5%)
Insufficient effect	16 (51.6%)	15 (62.5%)
Side effects	12 (38.7%)	6 (25.0%)
Ciclosporin	30/33 (90.9%)[a]	17/18 (94.4%)[a]
Sufficient effect	2 (6.7%)	2 (11.8%)
Insufficient effect	4 (13.3%)	8 (47.1%)
Side effects	24 (80.0%)	7 (41.2%)
Retinoids	16/21 (76.2%)[a]	14/28 (50.0%)[a]
Sufficient effect	0 (0%)	0 (0%)
Insufficient effect	6 (37.5%)	5 (35.7%)
Side effects	10 (62.5%)	9 (64.3%)

[a]Number of patients discontinued systemic treatment per total patients in each treatment group.

Prospective, multicentred randomized controlled trials are necessary to further determine the effectiveness of systemic therapies in LPP and FFA patients. Additionally, a standardized scoring system of disease activity and treatment response, along with side effect monitoring, is essential in elucidating the questions regarding LPP and FFA and draw definitive conclusions about the most effective treatment. Besides the focus on treatment responses, a better understanding of the pathogenesis might also help resolve questions regarding these hair disorders, as recent publications (5, 14, 23) mention a complex interaction between immune, hormonal, genetic, and environmental factors.

To summarize, this study suggests that MTX and CsA may be the most effective treatment options for LPP patients. For FFA patients, retinoids and CsA appear to have the best response rates. However, treatments with CsA and retinoids were often discontinued due to side effects compared with HCQ and MTX. Further studies

are needed to establish effective treatment protocols for LPP and FFA patients.

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REFERENCES

1. Kanti V, Rowert-Huber J, Vogt A, Blume-Peytavi U. Cicatricial alopecia. J Dtsch Dermatol Ges 2018; 16: 435–461. https://doi.org/10.1111/ddg.13498
2. Harries MJ, Paus R. The pathogenesis of primary cicatricial alopecias. Am J Pathol 2010; 177: 2152–2162. https://doi.org/10.2353/ajpath.2010.100454
3. Filbrandt R, Rufaut N, Jones L, Sinclair R. Primary cicatricial alopecia: diagnosis and treatment. CMAJ 2013; 185: 1579–1585. https://doi.org/10.1503/cmaj.111570
4. Olsen EA, Bergfeld WF, Cotsarelis G, Price VH, Shapiro J, Sinclair R, et al. Summary of North American Hair Research Society (NAHRS)-sponsored Workshop on Cicatricial Alopecia, Duke University Medical Center, February 10 and 11, 2001. J Am Acad Dermatol 2003; 48: 103–110. https://doi.org/10.1067/mjd.2003.68
5. Rongioletti F, Christana K. Cicatricial (scarring) alopecias: an overview of pathogenesis, classification, diagnosis, and treatment. Am J Clin Dermatol 2012; 13: 247–260. https://doi.org/10.2165/11596960-000000000-00000
6. Babahosseini H, Tavakolpour S, Mahmoudi H, Balighi K, Teimourpour A, Ghodsi SZ, et al. Lichen planopilaris: retrospective study on the characteristics and treatment of 291 patients. J Dermatolog Treat 2019; 30: 598–604. https://doi.org/10.1080/09546634.2018.1542480
7. Svigos K, Yin L, Fried L, Lo Sicco K, Shapiro J. A practical approach to the diagnosis and management of classic lichen planopilaris. Am J Clin Dermatol 2021; 22: 681–692. https://doi.org/10.1007/s40257-021-00630-7
8. Fechine COC, Valente NYS, Romiti R. Lichen planopilaris and frontal fibrosing alopecia: review and update of diagnostic and therapeutic features. An Bras Dermatol 2022; 97: 348–357. https://doi.org/10.1016/j.abd.2021.08.008
9. Soares VC, Mulinari-Brenner F, Souza TE. Lichen planopilaris epidemiology: a retrospective study of 80 cases. An Bras Dermatol 2015; 90: 666–670. https://doi.org/10.1590/abd1806-4841.20153923
10. Rajan A, Rudnicka L, Szepietowski JC, Lallas A, Rokni GR, Grabbe S, et al. Differentiation of frontal fibrosing alopecia and lichen planopilaris on trichoscopy: a comprehensive review. J Cosmet Dermatol 2022; 21: 2324–2330. https://doi.org/10.1111/jocd.14457
11. Iorizzo M, Tosti A. Frontal fibrosing alopecia: an update on pathogenesis, diagnosis, and treatment. Am J Clin Dermatol 2019; 20: 379–390. https://doi.org/10.1007/s40257-019-00424-y
12. Ramot Y, Bertolini M, Boboljova M, Uchida Y, Paus R. PPAR-gamma signalling as a key mediator of human hair follicle physiology and pathology. Exp Dermatol 2020; 29: 312–321. https://doi.org/10.1111/exd.14062
13. Harnchoowong S, Suchonwanit P. PPAR-gamma agonists and their role in primary cicatricial alopecia. PPAR Res 2017; 2017: 2501248. https://doi.org/10.1155/2017/2501248
14. Senna MM, Peterson E, Jozic I, Cheret J, Paus R. Frontiers in lichen planopilaris and frontal fibrosing alopecia research: pathobiology progress and translational horizons. JID Innov 2022; 2: 100113. https://doi.org/10.1016/j.xjidi.2022.100113
15. Racz E, Gho C, Moorman PW, Noordhoek Hegt V, Neumann HA. Treatment of frontal fibrosing alopecia and lichen planopilaris: a systematic review. J Eur Acad Dermatol Venereol 2013; 27: 1461–1470. https://doi.org/10.1111/jdv.12139
16. Nasimi M, Ahangari N, Lajevardi V, Mahmoudi H, Ghodsi SZ, Etesami I. Quality of life and mental health status in patients with lichen planopilaris based on Dermatology Life Quality Index and General Health Questionnaire-28 questionnaires. Int J Womens Dermatol 2020; 6: 399–403. https://doi.org/10.1016/j.ijwd.2020.09.005
17. Suchonwanit P, Pakornphadungsit K, Leerunyakul K, Khunkhet S, Sriphojanart T, Rojhirunsakool S. Frontal fibrosing alopecia in Asians: a retrospective clinical study. Int J Dermatol 2020; 59: 184–190. https://doi.org/10.1111/ijd.14672
18. Lyakhovitsky A, Amichai B, Sizopoulou C, Barzilai A. A case series of 46 patients with lichen planopilaris: demographics, clinical evaluation, and treatment experience. J Dermatolog Treat 2015; 26: 275–279. https://doi.org/10.3109/09546634.2014.933165
19. Cantwell HM, Wieland CN, Proffer SL, Imhof RL, Torgerson RR, Tolkachjov SN. Lichen planopilaris in men: a retrospective clinicopathologic study of 19 patients. Int J Dermatol 2021; 60: 482–488. https://doi.org/10.1111/ijd.15285
20. Bulbul Baskan E, Yazici S. Treatment of lichen planopilaris: methotrexate or cyclosporine A therapy? Cutan Ocul Toxicol 2018; 37: 196–199. https://doi.org/10.1080/15569527.2017.1382503
21. Errichetti E, Figini M, Croatto M, Stinco G. Therapeutic management of classic lichen planopilaris: a systematic review. Clin Cosmet Investig Dermatol 2018; 11: 91–102. https://doi.org/10.2147/CCID.S137870
22. Ho A, Shapiro J. Medical therapy for frontal fibrosing alopecia: a review and clinical approach. J Am Acad Dermatol 2019; 81: 568–580. https://doi.org/10.1016/j.jaad.2019.03.079
23. Kerkemeyer KLS, Eisman S, Bhoyrul B, Pinczewski J, Sinclair RD. Frontal fibrosing alopecia. Clin Dermatol 2021; 39: 183–193. https://doi.org/10.1016/j.clindermatol.2020.10.007
24. Gamret AC, Potluri VS, Krishnamurthy K, Fertig RM. Frontal fibrosing alopecia: efficacy of treatment modalities. Int J Womens Health 2019; 11: 273–285. https://doi.org/10.2147/IJWH.S177308
25. Chiang C, Sah D, Cho BK, Ochoa BE, Price VH. Hydroxychloroquine and lichen planopilaris: efficacy and introduction of Lichen Planopilaris Activity Index scoring system. J Am Acad Dermatol 2010; 62: 387–392. https://doi.org/10.1016/j.jaad.2009.08.054
26. Holmes S, Ryan T, Young D, Harries M. Frontal Fibrosing Alopecia Severity Index (FFASI): a validated scoring system for assessing frontal fibrosing alopecia. Br J Dermatol 2016; 175: 203–207. https://doi.org/10.1111/bjd.14445