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Review Article

Treatment of Frontal Fibrosing Alopecia

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Introduction. Frontal fibrosing alopecia (FFA) is known as a lymphocytic primary cicatricial alopecia. The main characteristic of FFA is progressive frontotemporal hairline recession. The pathogenesis of FFA is not completely understood. Destructing the stem cells of the epithelial hair follicles causes permanent hair loss and seems to be the main cause of FFA. Studies have reported significantly decreased quality of life in patients with hair loss. On the other hand, late diagnosis and treatment of FFA can decrease the success rate of the treatment. In this regard, different topical and systemic therapies have been developed to resolve the symptoms; however, only a partial response to treatment is usually achieved. We conducted a systematic review of the literature to identify the effectiveness of the available treatment modalities used for FFA patients and the related outcomes. *Methods*. On April 2022, we made a wide systematic computer-assisted search of *PubMed* and *Google Scholar* databases, using "frontal fibrosing alopecia" and "treatment" keywords. We scanned 1,514 articles. All the studies concerning a therapeutic regimen for FFA were included. After removing duplicate studies, 50 studies containing the therapeutic regimen of 1,478 FFA patients were included in this review. *Results*. The 5-alpha-reductase inhibitors (oral finasteride/dutasteride) were the most used medications (usually prescribed as a combination therapy with other medications). Topical corticosteroids were the second commonly used medication for the treatment of FFA. Systemic corticosteroids seem to be ineffective in improving FFA progression. Oral isotretinoin (or alitretinoin) had the most promising effect on improving facial papules of FFA patients with a 92% rate of facial papule improvement. *Conclusion*. In our review, intralesional corticosteroid injection and 5-alpha-reductase inhibitors (finasteride/dutasteride) were reported as the most effective treatment modalities. Oral isotretinoin (or alitretinoin) is considered as the most promising treatment for improving facial papules in the context of FFA. However, it had minimal effects on hair regrowth or stabilization of hairline recession in FFA patients.

1. Introduction

Frontal fibrosing alopecia (FFA), first described by Kossard in 1994, is known as a lymphocytic primary cicatricial alopecia [1]. As reported in the literature, most of the patients affected by FFA are postmenopausal women [2], although it has also been reported in men and premenopausal women [1, 3–5]. The main characteristics of FFA are progressive frontotemporal hairline recession, eyebrow hair loss, body hair loss, and perifollicular erythema and hyperkeratosis [1], which are commonly accompanied by itching, burning, or pain [6]. In FFA, infundibulum and isthmus of the hair follicles are surrounded by lymphocytic infiltration and fibrosis, often with sebaceous gland loss. According to the histological presentation, FFA is assumed to be a variant of lichen planopilaris (LPP), which is known by multifocal patches of alopecia, pruritus, burning, and tenderness in the affected area [3]; however, this assumption is still controversial.

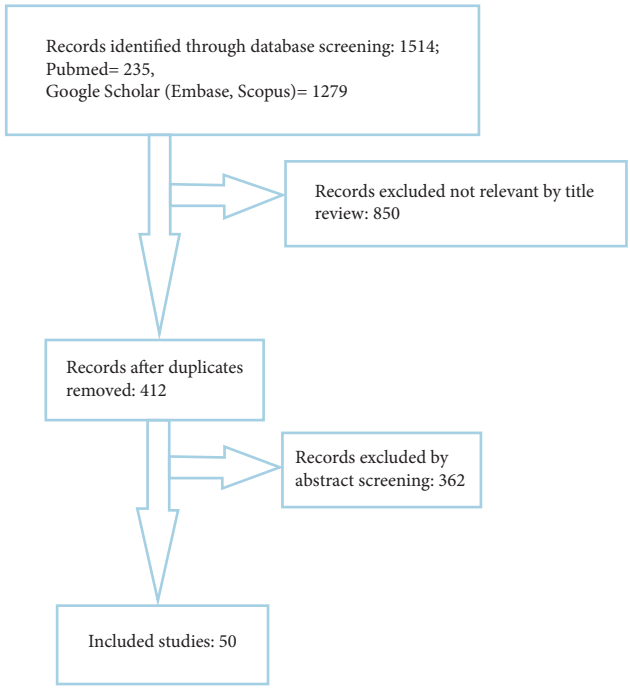

Figure 1: Flow diagram for literature search and screening.

The pathogenesis of FFA is not completely understood. The destruction of the stem cells of the epithelial hair follicles, where the infiltration of the inflammatory cells primarily happens, causes permanent hair loss, and seems to be the main cause of FFA. The proinflammatory cytokines such as interferons, the increased apoptotic response, and the collapse of the relative immune privilege of the hair follicle could be considered as trigger to an ongoing inflammatory response, leading to the mentioned stem cell destruction [7]. Also, the possible pathogenetic role of androgens has been proposed, as well as the theory that the melanocyte of the upper hair follicle might represent the antigenic target in FFA [8].

Beside this, studying gene expressions has indicated a defective lipid metabolism signaling pathway in LPP, which is a vital part of sebaceous gland function [9].

Studies have reported a significantly decreased quality of life in patients with hair loss. Loss of self-confidence and low self-esteem are the most common psychosocial findings in women with alopecia [10]. On the other hand, late diagnosis and treatment of FFA can decrease the success rate of the treatment [11].

In this regard, different topical and systemic therapies have been developed to resolve the symptoms [11]; however, only a partial response to treatment is usually achieved [12].

Numerous studies have tried to represent a better insight into or management of FFA. We conducted a systematic review of the literature to identify the effectiveness of the available treatment modalities used for FFA patients and the related outcomes.

2. Methods

On April 2022, we made a wide systematic computer-assisted search of *PubMed* and *Google Scholar (Embase, Scopus)* data base, using "frontal fibrosing alopecia treatment" keyword. We scanned 1,514 studies (Figure 1).

All types of studies, including case reports, case series, case-control studies, randomized controlled trials, cohort and cross-sectional studies, and retrospective and prospective observational studies, were reviewed. Furthermore, we checked the references of included studies and also review articles concerning the FFA, and related studies were included. On data acquirement, no language limitation was applied.

The studies reporting no treatment or outcome of the treatment, no histopathological diagnosis of FFA, or those concerning different topic were excluded. All the studies concerning a therapeutic regimen for FFA were included.

After removing duplicate studies, 50 studies containing the therapeutic regimen of 1,478 FFA patients were included in our review. The characteristics of studies, including the name of the first author, type of study, number of patients, mean age of the patients, diagnosis, evidence of histology, the mean of disease duration, administered therapeutic regimens, outcome evaluation criteria, response to treatment, and follow-up duration, are summarized in Table 1 [1, 3, 4, 13–59].

When first a treatment modality was administered, and later another one, both of these treatments were included.

There are no standard criteria for measuring the treatment outcome of FFA. So, the studies used different qualitative and quantitative indices for measuring the treatment outcomes of the patients. In order to evaluate the response to treatments, we classified the results of studies as "improved," "stabilized," and "worsened" groups, according to the hired outcome measurement index. When patients experienced improvement, including hair regrowth, symptom recovery, or any improvement in the course of disease, it was classified as "improved." When a halt in hair loss or a steady state of the disease was observed, it was classified as "stabilized." When no improvement or stabilization was achieved or worsening of the disease course was reported, it was classified as "worsened."

In Table 1, where the "*response to treatment*" chart is reporting one outcome or the "*Duration*" chart is reporting a single period of time, it refers to the combination of administered treatment modalities; if not, the period of consumption and outcome of each treatment modality is noted separately.

3. Results

Various criteria were hired to evaluate the outcome of therapeutic regimens used for FFA treatment; however, response to treatment was different among the studies (summarized in Table 1). The efficacy of treatment modalities hired for treating FFA is summarized in Table 2.

Overall, 1,478 FFA patients were described. They received different therapeutic regimens as monotherapy or combination therapy.

Oral finasteride (1, 2.5, or 5 mg per day) or dutasteride (0.5 mg per day) were the most used medications (508 patients) (usually prescribed as a combination therapy with

Table 1: Details of treatment modalities hired for FFA treatment.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Gkini et al. [13]/ retrospective analysis	40 (f)/ 65.88 ± 8.18 y	FFA (yes)/not available	(i) ITAIs1 (intralesional triamcinolone acetonide injections) (on scalp: 10 mg/ml (10%)/on eyebrow: 5 mg/ml (5%))	(i) 0.1 ml/cm^2 (on scalp)/0.125 ml/cm^2 (on eyebrow) ITAIs was repeated every 3 months	4 sessions of ITAIs	Management of hairline recession	Stabilized ($n = 40$) (Stop of hair loss with no more disease progression at f/u sessions)	6 m–4 y
Pirmez et al. [14]/ prospective observational study	3 (f)/49–53 y	FFA (yes)/NA	(i) Oral isotretinoin	(i) 20 mg/day for 1 month then titrated to 0.5 mg/kg/day for 2 months (40 mg/day in all 3 patients)	3 m	Improvement of facial papules	Improved ($n = 3$) (Facial papules had completely vanished or considered minimal)	3 m
Batra et al. [15]/case report	1 (f)/45 y	FFA (yes)/4 y	(i) Oral finasteride (ii) Oral HCQ (Hydroxychloroquine) (iii) ITAIs (iv) Topical minoxidil 5% solution	(i) 5 mg/D (ii) 200 mg/BD (iii) Triamcinolone acetonide (2.5 mg/mL), monthly (iv) 1 drop/BD	17 m	Hair regrowth along the hairline and trichoscopy	Improved ($n = 1$) (elimination of hyperkeratosis and inflammation on trichoscopy, and hair regrowth was seen)	NA
Diehl et al. [16]/case report	1 (f)/56 y	FFA (yes)/3 y	(i) HCQ (ii) ITAIs (iii) Doxycycline monohydrate (iv) Topical minoxidil 5%	(i) NA (ii) Triamcinolone 3 mg/mL (with 1 mm given monthly in each temporal area) (iii) 100 mg BD (iv) BD	2 m	Hair regrowth	Worsened ($n = 1$) (there was only some vellus hair growth at the site of applying minoxidil solution)	NA
Lee et al. [17]/case report	1 (f)/63 y	FFA (yes)/4 m	(i) Oral alitretinoin	(i) 30 mg/D	5 m	Improvement of facial papules	Improved ($n = 1$) (Facial papules had completely vanished)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Panchaprateep et al. [18]/ retro-prospective cohort study	46 (f)/61 y	FFA (yes)/1–5 y	(i) Monotherapy with topical treatments (topical steroids, topical tacrolimus, topical pimecrolimus, topical minoxidil, topical retinoids) ($n = 9$, 19.6%) (ii) Finasteride 5 mg/day (or dutasteride 0.5 mg/day) with topical treatment ($n = 23$, 50%) (iii) HCQ (200–400 mg/day) with topical treatment ($n = 10$, 21.7%) (iv) Other systemic treatment (e.g. cyclosporin A,doxycycline) with topical treatment ($n = 4$, 8.7%)	As mentioned	NA	Hair regrowth along the hairline	(i) Improved ($n = 3$, 33.3%)/stabilized ($n = 6$, 66.7%) (ii) Improved ($n = 6$, 26.1%)/stabilized ($n = 15$, 65.2%)/ worsened ($n = 2$, 8.7%) (iii) Improved ($n = 3$.30%)/stabilized ($n = 6$.60%)/worsened ($n = 1$.10%) (iv) Improved ($n = 1$.25%)/stabilized ($n = 2$.50%)/worsened ($n = 1$.25%)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Suchonwanit et al. [19]/retrospective clinical study	56 (f: 54, m: 2)/51.3 y	FFA (yes)/6.5 (1–15) y	(i) Topical steroids with HCQ ($n = 29$) (ii) Topical steroids with finasteride ($n = 15$) (iii) Intralesional steroids with HCQ ($n = 10$) (iv) High-potency topical corticosteroids (v) HCQ ($n = 4$) (vi) Intralesional steroids ($n = 4$) (vii) HCQ with doxycycline ($n = 8$) (viii) Topical steroids with intralesional steroids ($n = 7$) (ix) Topical tacrolimus with HCQ ($n = 3$) (x) HCQ with pioglitazone ($n = 2$) (xi) Topical steroids with dutasteride ($n = 1$) (xii) HCQ with methotrexate ($n = 1$) (xiii) Topical steroids with acitretin ($n = 1$)	NA	NA	Management of hairline recession and hair loss/decrease of the symptoms	(i) Stabilized ($n = 23$, 79.3%) (ii) Stabilized ($n = 11$, 73.3%) (iii)Stabilized ($n = 5.50\%$) (iv) Worsened (v) Worsened (vi) Worsened (vii) Worsened (viii) Worsened (ix) Worsened (x) Worsened (xi) Worsened (xii) Worsened (xiii) Worsened	1–15 y

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Mahmoudi et al. [20]/ randomized controlled trial	38 (f: 36, m: 2)/46 ± 9.4 y	FFA (yes)/NA	(i) isotretinoin (20 mg/day) with topical treatments (consisted of: topical clobetasol 0.05% (for 5 days) followed by tacrolimus 0.1% (for 2 days), after two weeks, a weekly cycle of tacrolimus 0.1% (for 5 days) and clobetasol 0.05% (for 2 days)) ($n = 19$) (ii) Monotherapy with topical treatments ($n = 19$)	As mentioned	6 m	Hair regrowth along the hairline and vertex/improvement of facial papules	(i) Improved (ii) Worsened	6 m
Pindado et al. [21]/ retrospective observational study	224 (f: 222, m: 2)/NA	FFA (yes)/NA	(i) Capsule dutasteride 0.5 mg ($n = 148$, 66.1%) (ii) Finasteride ($n = 9$, 4%) (iii) HCQ ($n = 6$, 2.7%) (iv) Doxycycline ($n = 2$, 1.3%) (v) Oral isotretinoin ($n = 2$, 0.9%) (vi) Topical minoxidil 5% (all patients) (vii) Clobetasol propionate 0.05% solution (all patients)	(i) 1 to 7 caps pre week (ii) 2.5–5 mg/day (iii) 200–400 mg/day (iv) 100 mg/day (v) 5–20 mg/day (vi) 5 nights a week (vii) Twice weekly	12 m≤	Stabilization of the hairline recession	(i) Stabilized (ii) Stabilized (iii) Worsened (iv) Worsened (v) Worsened (vi) Worsened (vii) Worsened	24 (12–108) m
Pirmez and Spagnol Abraham [22]/case series	7 (f)/35–65 y	FFA (yes)/NA	(i) Low dose oral minoxidil	(i) Initial dose 0.5 mg ($n = 2$) 0.75 mg ($n = 2$) 1.25 mg ($n = 3$) daily/ at month 3, the dose was increased to 2.5 mg/day in 5 patients	5 m	Eyebrow regrowth	(i) Improved (complete ($n = 2$) and partial ($n = 5$) regrowth of eyebrow was seen)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Pham et al. [23]/case series	3 (f: 2, m: 1)/ 45 y	FFA (yes)/3.66 y	(i) Oral isotretinoin 30 mg/day + intralesional triamcinolone 5 mg/mL every 6 to 8 weeks (ii) Oral isotretinoin 20 mg/day + intralesional triamcinolone 5 mg/mL every 6 to 8 weeks + topical clobetasol 0.05% solution daily (iii) Oral isotretinoin 20 mg BD + topical minoxidil 5% BD + ketoconazole shampoo 2% topically 3 times per week + fluocinonide 0.05% solution topically BD + intralesional triamcinolone 5 mg/mL every 6 to 8 weeks	As mentioned	6 m≤	Improvement of facial papules	Improved ($n = 3$) (significant decrease in the number and size of facial papules, regrowth of eyebrows, hairline stability was seen)	18–24 m
Stumpf et al. [24]/case report	1 (f)/53 y	FFA (no)/3 y	(i) Methotrexate	(i) 20 mg once a week	7 m	Improvement of fronto-temporal hairline recession	(i) Stabilized	NA
Cid et al. [25]/ observational retrospective cross-sectional study	75 (f: 73, m: 2)/61 y	FFA (yes)/4 y	(i) ITAIs ($n = 6$) (ii) HCQ ($n = 5$) (iii) Finasteride ($n = 2$) (iv) Oral corticosteroids (prednisone) ($n = 1$) (v) Oral isotretinoin ($n = 1$) (vi) Dutasteride ($n = 14$)	(i) 8 mg/mL (ii) 200–400 mg/d (iii) 2.5 mg/d (iv) 50 mg (v) 20 mg/d (vi) 0.5 mg/d (1–3 times per week)	10 m	Stabilization of hairline recession	(i) Stabilized ($n = 2$, 33%) (ii) Stabilized ($n = 5$, 100%) (iii) Stabilized ($n = 1$, 50%) (iv) Worsened (v) Worsened (vi) Stabilized ($n = 9$, 64.2%)	11.5 m
Cardona et al. [26]/ case series	5 (f)/41.4 y	FFA (yes)/4 y	(i) Oral isotretinoin	(i) 10 mg/d	3–24 m	Improvement of facial papules	(i) Improved ($n = 5$) (Rapid improvement of the papules, with persistence of the other skin findings)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Murad and Bergfeld [27]/case series	3 (f)/53.3 y	FFA (yes)/ 6 m–15 y	(i) HCQ ($n = 3$) (ii) Topical minoxidil 5% ($n = 3$) (iii) Clobetasol propionate (0.05%) lotion ($n = 3$) (iv) Topical bimatoprost ophthalmic solution 0.03% ($n = 3$)	(i) 200 mg BD (ii) Daily (iii) Daily (iv) BD	(i) 6 m< (ii) 6 m< (iii) 6 m< (iv) 9 m<	Regrowth of eyebrows	(i) Worsened ($n = 3$) (ii) Worsened ($n = 3$) (iii) Worsened ($n = 3$) (iv) Improved ($n = 2$)	NA
Özcan et al. [28]/case report	1 (f)/44 y	FFA (yes)/NA	(i) Clobetasol propionate lotion 0.05% (on the scalp) (ii) Prednisolone cream 0.125% (on the eyebrows) (iii) HCQ (iv) Topical minoxidil 5% lotion (on the scalp) (v) ITAIs (vi) PRP (platelet rich plasma) injection	(i) BD (ii) BD (iii) 400 mg/d (iv) BD (v) (Into the eyebrows: 2.5 mg/ml, and fronto-temporal hairline: 5 mg/ml) (6 treatments with 1-month interval) (vi) (0.1 ml/cm^2, 5 treatments with 1-month interval)	9 m	Improvement of frontotemporal hairline recession	(i) Worsened (ii) Worsened (iii) Worsened (iv) Worsened (v) Worsened (vi) Improved (improvement of disease symptoms with no more hair loss)	NA
Peterson et al. [29]/ retrospective review	7 (m)/54 y	FFA (yes)/NA	(i) Doxycycline (ii) HCQ (iii) Naltrexone (iv) Pioglitazone (v) Finasteride (vi) Topical minoxidil 5% (vii) Topical tacrolimus 0.3% (viii) Clobetasol solution 0.05% (ix) Clobetasol 0.05% shampoo (x) ITAIs (xi) PRP injection	(i) 100 mg daily (ii) 200 mg daily (iii) 4.5 mg daily (iv) 15 mg daily (v) 1 mg daily (vi) BD (vii) Daily (viii) Daily (ix) Three times weekly (x) NA (xi) NA	14 m (1–51)	Stabilization of hair loss/trichoscopy/ resolution of symptoms	Improved ($n = 7$) (improvement of disease symptoms with no more hair loss, one patient experienced minor regrowth of eyebrows)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Campbell and McKenna [30]/case report	1 (f)/48 y	FFA (yes)/7 y	(i) Oral isotretinoin	(i) 20 mg/day	6 m	Improvement of facial papules	(i) Improved (overall reduction and flattening of the papules)	2 y
Trindade de Carvalho [31]/case report	1 (f)/73 y	FFA (yes)/ several years	(i) ITAIs	(i) Triamcinolone acetonide 5 mg/mL	(i) 58 m	Improvement of hairline recession	(i) Worsened	13 m
			(ii) Oral corticosteroids (prednisone)	(ii) 15 mg daily	(ii) 3 m		(ii) Worsened	
			(iii) Infrared light	(iii) (15 sessions)	(iii) 42 m		(iii) Worsened	
			(iv) HCQ	(iv) 400 mg daily	(iv) 18 m		(iv) Worsened	
			(v) Ciclosporin	(v) 50 mg daily	(v) 6 m		(v) Worsened	
			(vi) Minocycline	(vi) 100 mg daily	(vi) 6 m		(vi) Worsened	
			(vii) Doxycycline	(vii) 5 mg daily	(vii) 6 m		(vii) Worsened	
			(viii) Tofacitinib	(viii) 50 mg daily	(viii) 3 m		(viii) Worsened	
			(ix) Flutamide	(ix) 1–2 mg/day	(ix) 65 m		(ix) Worsened	
			(x) Topical minoxidil	(x) 0.5 mg daily	(x) 14 m		(x) Improved	
			(xi) Dutasteride	(xi) 100 mg at week 0, 4 and 12 (weekly)	(xi) NA		(xi) Improved	
			(xii) Tildrakizumab (interleukin-23 monoclonal antibody)				(xii) Improved	
Starace et al. [32]/case series	65 (f)/62.5 y	FFA (yes)/4.3 y	(i) Intramuscular triamcinolone acetonide ($n = 15$, 23.1%)	(i) 0.5 mg/kg/month	6 m≤	Improvement of hairline recession	Improved (systemic agents in regards to hair loss improvement: 75%, topical agents in regards to symptoms improvement: 91%)	6 m≤
			(ii) ITAIs ($n = 3$, 4.5%)	(ii) 3 ml every 6 weeks)				
			(iii) HCQ ($n = 10$, 15.4%)	(iii) 400 mg/da				
			(iv) Oral finasteride (2.5 mg/day) or dutasteride (0.5 mg/day) ($n = 45$ patients, 69.3%)	(iv) As mentioned				
			(v) Topical clobetasone propionate 0.05 ($n = 15$, 23.1%)	(v) Daily				
			(vi) Topical tacrolimus 0.1% ($n = 40$, 61%)	(vi) Daily				
			(vii) Topical pimecrolimus cream ($n = 20$, 13%)	(vii) Daily				

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Letulé et al. [33]/ retrospective study	72 (f: 70, m: 2)/62 y	FFA (yes)/NA	(i) HCQ (ii) Systemic retinoids ($n = 4$, 5.6%) (iii) Tacrolimus ($n = 13$, 18.1%) (iv) Topical pimecrolimus 1% ($n = 53$, 73.6%) (v) Topical high-potency steroids (all patients) (clobetasol propionate (81.9%, $n = 59$) and betamethasone valerate (27.8%, $n = 20$))	(i) 200 to 400 mg/day (ii) Daily (iii) Daily (iv) Daily (v) Daily	NA	Improvement of hairline recession	(i) Worsened (ii) NA (iii) NA (iv) Improved (64.6%) (in combination with high-potency steroids)	20 m
Flores Terry et al. [34]/case report	2 (f)/43.5 y	FFA (yes)/4 y	(i) Oral isotretinoin	(i) 10 mg/day	6 m	Improvement of facial papules	(i) Improved ($n = 2$)	NA
Murad and Bergfeld [35]/case report	1 (f)/48 y	FFA (yes)/6 m	(i) HCQ (ii) Clobetasol propionate (0.05%) lotion (iii) Tacrolimus ointment (0.1%) (iv) Topical bimatoprost ophthalmic solution 0.03%	(i) 200 mg BD (ii) Daily (iii) Daily (iv) BD	(i) 14 m (ii) 14 m (iii) 14 m (iv) 6 m	Improvement of scalp alopecia/regrowth of eyebrows	(i) Stabilized (ii) Stabilized (iii) Stabilized (iv) Improved (eyebrows regrowth)	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Strazzulla et al. [36]/ retrospective review	92 (f: 90, m: 2)/55 y	FFA (yes)/NA	(i) ITAIs (ii) HCQ (iii) Antibiotics (doxycycline, tetracycline, or minocycline) (iv) Methotrexate (v) Spironolactone (vi) Finasteride/dutasteride (vii) Tacrolimus, 0.3% (in cetaphil cleanser) (viii) Hydrocortisone butyrate, 0.1% solution (ix) Topical minoxidil 5% (x) Clobetasol propionate, 0.05% lotion or betamethasone dipropionate 0.05% lotion	NA	10.4 $m\leq$	No further hairline recession, eyebrow loss, or evidence of active inflammation	(i) Stabilized (71.7%, $n=66$) (ii) Stabilized (34.8%, $n=32$) (iii) Stabilized (70.7%, $n=65$) (iv) Worsened (v) Worsened (vi) Stabilized (26.1%, $n=24$) (vii) Stabilized (41.3%, $n=38$) (viii) Stabilized (54.3%, $n=50$) (ix) Stabilized (67.4%, $n=62$) (x) Stabilized (23.9%, $n=22$)	21.4 m

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Zhang et al. [37]/ retrospective review	29 (f: 28, m: 1)/55.4 y	FFA (yes)/NA	(i) Topical steroids ($n = 21$,.72%) (ii) HCQ ($n = 16.55\%$) (iii) Intralesional steroids ($n = 11.38\%$) (iv) Topical pimecrolimus (or tacrolimus) ($n = 6.21\%$) (v) Topical minoxidil ($n = 3.10\%$) (vi) Antibiotics (doxycycline, tetracycline, or minocycline) ($n = 10.30\%$) (vii) Bimatoprost ($n = 1.3\%$) (viii) Methotrexate ($n = 1.3\%$) (ix) Oral isotretinoin ($n = 1.3\%$) (x) Finasteride (or dutasteride) ($n = 2.6\%$)	NA	NA	Hair regrowth or hair loss stabilization	(i) Stabilized ($n = 11$) (ii) Stabilized ($n = 10$) (iii) Worsened (iv) Stabilized ($n = 5$) (v) Worsened (vi) Worsened (vii) NA (viii) NA (ix) NA (x) NA	NA
Georgala et al. [38]/ prospective uncontrolled study	13 (f)/61 y	FFA (yes)/2–9 y	(i) Oral dutasteride	(i) 0.5 mg/day	12 m	Stabilization or reduction of the hairline recession	Stabilized (complete arrest of the FFA progression in 6 pts (46.1%), partial hair regrowth in 2 pts (15.3%), decreasing hair loss in 5 others) (significant eyebrow regrowth in 5 pts (71.4%), others remained stable)	18 m
Moreno et al. [39]/ retrospective analysis	106 (f)/61.4 y	FFA (yes)/18 m	(i) Oral dutasteride ($n = 106$) (ii) Topical clobetasol 17-propionate foam ($n = 106$)	(i) 0.5 mg 3 times a week (ii) 0.05% twice weekly	12 m	Improvement of hairline recession	(i) Worsened (stabilization was reported in 37.3% of the patients)	12 m

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Galván et al. [1]/ retrospective analysis	335 (f: 343, m: 12)/61 y	FFA (yes)/5.3 y	(i) Dutasteride ($n = 18$)	(i) 0.5 mg weekly	NA	Improvement of hairline recession	(i) Improved ($n = 8.44\%$)/Stabilized ($n = 10.56\%$)	2.1 y
			(ii) Finasteride ($n = 98$)	(ii) 2.5–5 mg daily			(ii) Improved ($n = 48.47\%$)/ Stabilized ($n = 50.53\%$)	
			(iii) HCQ ($n = 52$)	(iii) 200–400 mg daily			(iii) Improved ($n = 8.15\%$)/stabilized ($n = 32.59\%$)/worsened ($n = 12.22\%$)	
			(iv) Intralesional corticosteroids ($n = 114$)	(iv) Every 3–6 months			(iv) Improved ($n = 44.34\%$)/ stabilized ($n = 64.49\%$)/ worsened ($n = 6.5\%$)	
			(v) Topical corticosteroids and topical minoxidil	(v) NA				
Ladizinski et al. [40]/ retrospective analysis	19 (f)/NA	FFA (yes)/NA	(i) Dutasteride ($n = 10$)	(i) 0.5 mg daily for 2 weeks then 0.5 mg weekly	23 m	Stabilization of hair loss	(i) Stabilized ($n = 7.70\%$)	2 y
			(ii) Finasteride ($n = 3$)	(ii) 1–2.5 mg daily			(ii) Stabilized ($n = 1.33\%$)	
			(iii) Methotrexate ($n = 3$)	(iii) 15–25 mg weekly			(iii) Stabilized ($n = 1.50\%$)	
			(iv) HCQ 400 mg daily ± topical tacrolimus or class I corticosteroids ($n = 2$)	(iv) As mentioned			(iv) Stabilized ($n = 1.33\%$)	
			(v) Minocycline + topical tacrolimus ($n = 2$)	(v) NA			(v) Stabilized ($n = 1.50\%$)	
			(vi) Imiquimod + topical corticosteroid class I ($n = 2$)	(vi) NA			(vi) Stabilized ($n = 1.50\%$)	
Donovan et al. [41]/ retrospective review	11 (f)/50.63 y	FFA (yes)/3 y	(i) ITAIs ($n = 11$)	(i) Triamcinolone acetonide 10 mg/ml (0.125 mL per eyebrow)	3–72 m	Regrowth of eyebrows	Improved ($n = 10$, 90.9%)	1–5 y
			(ii) HCQ ($n = 11$)	(ii) 200 mg BD			(Significant eyebrow regrowth was seen)	

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Samrao et al. [42]/ retrospective review	36 (f: 35, m: 1)/60 y	FFA (yes)/1 y	(i) HCQ ($n = 15$) (ii) Doxycycline ($n = 4$) (iii) Mycophenolate mofetil ($n = 5$)	NA	(i) 12 m (ii) 18 m (iii) 6 m	Decreasing the LPPAI (lichen planopilaris activity index) score	(i) Improved ($n = 11$, 68.8%) (ii) Improved ($n = 2.50\%$) (iii) Improved ($n = 3.60\%$)	12 m
Chiang et al. [43]/ retrospective review	7 (NA)/62 y	FFA (yes)/NA	(i) HCQ	(i) 200 mg BD	12 m	Decreasing the LPPAI score	(i) Improved ($n = 6$, 88%)	1 y<
Tosti et al. [44]/ retrospective review	11 (f)/62 y	FFA (yes)/5 y	(i) Finasteride 2.5 mg daily + topical minoxidil 2% BD ($n = 8$) (ii) Intramuscular triamcinolone acetonide 40 mg every 3 weeks + topical minoxidil 2% BD ($n = 3$)	As mentioned	18 m	Disease stabilization	(i) Stabilized ($n = 4$) (ii) Worsened	12–30 m
Moreno and Camacho Martinez [45]/retrospective review	15 (f)/45–79 y	FFA (yes)/2.5 y	(i) Finasteride ($n = 7$) (ii) Topical minoxidil 5% ($n = 7$) (iii) ITAIs ($n = 15$)	(i) 2.5 mg daily (ii) BD (iii) Triamcinolone acetonide 20 mg/mL (1 mg/2 cm^2 with 1/10 dilution) every 3 months	NA	Stabilizatig the disease progression and increasing hair density	Improved (antiandrogenic drugs were more likely associated with increasing the hair density)	1–3.5 y

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Kossard et al. [3]/ retrospective review	16 (f)/66.8 y	FFA (yes)/1–10 y	(i) Oral corticosteroids (prednisone) ($n = 4$) (ii) Chloroquine phosphate ($n = 3$) (iii) Oral isotretinoin ($n = 1$) (iv) Ultramicronized griseofulvin ($n = 1$) (v) Topical moderately potent corticosteroids ($n = 9$) (vi) Topical retinoic acid ($n = 2$) (vii) Topical minoxidil 2% ($n = 2$) (viii) Intralesional corticosteroids ($n = 1$) (ix) Hormone replacement therapy ($n = 8$)	(i) 50 mg/day (ii) 150 mg/day (iii) 50 mg/day (iv) 330 mg/day (v) NA (vi) NA (vii) NA (viii) NA (ix) NA	(i) 1 m (ii) 3–9 m (iii) 2 m (iv) 1 m (v) NA (vi) NA (vii) NA (viii) NA (ix) NA	Slowing down the hair loss	Worsened (medications had no effect on hair loss of progressive FFA patients)	2–5 y
Tan and Messenger [46]/retrospective review	18 (f)/55.5 y	FFA (yes)/NA	(i) ITAIs ($n = 12$) (ii) Topical tacrolimus 0.1% ($n = 5$) (iii) HCQ ($n = 3$) (iv) Clobetasol (v) Topical minoxidil	(i) Triamcinolone acetonide 10 mg/mL (ii) NA (iii) NA (iv) NA (v) NA	NA	Progression of frontotemporal hairline recession	(i) Improved ($n = 8$) (ii) NA (iii) Improved ($n = 1$) (iv) Improved (v) Improved	3 m–15 y
Katoulis et al. [47]/ case report	1 (f)/55 y	FFA (yes)/1 y	(i) Oral dutasteride (ii) Pimecrolimus 1% cream	(i) 0.5 mg daily (ii) BD	6 m	Eyebrows and frontoparietal hair regrowth	Improved (significant hair regrowth was seen)	6 m
Donovan [48]/case report	1 (f)/51 y	FFA (yes)/9 y	(i) Oral finasteride	(i) 2.5 mg daily	1 y	Frontotemporal hair regrowth and decreasing erythema and skin atrophy	Improved	1 y
Faulkner et al. [4]/ case report	1 (f)/45 y	FFA (yes)/18 m	(i) Topical fluocinolone acetonide 0.025% (ii) Topical clobetasol proprionate 0.05% cream	(i) BD (ii) BD (on the face)	12 m	Improvement of skin lesions and hair loss	Improved	1 y
Pérez-Rodríguez et al. [49]/case report	1 (f)/57 y	FFA (yes)/3 y	(i) Oral dutasteride (ii) Topical pimecrolimus 1%	(i) 0.5 mg daily (ii) BD	(i) 8 m (ii) 3 m	Improvement of erythema and hair regrowth	Improved	13 m

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Contin et al. [50]/case series	4 (f)/60.5 y	FFA (yes)/NA	(i) HCQ	(i) NA	4.5 y	Disease activity level	(i) Worsened ($n = 4$)	NA
Dlova et al. [51]/ retrospective review	20 (f: 19, m: 1)/42 y	FFA (yes)/NA	(i) HCQ (ii) Topical medications (clobetasol diproprionate, tacrolimus 0.1%, minoxidil 2%)	(i) 200 mg BD (ii) NA	6–12 m	Frontotemporal hair regrowth	Worsened (disease stabilization was achieved in only 5 pts)	2 y
Cranwell and Sinclair [52]/case report	1 (f)/46 y	FFA (yes)/10 m	(i) HCQ (ii) Methotrexate (iii) ITAIs (iv) Dutasteride (v) Oral minoxidil	(i) 400 mg daily (ii) 20 mg (iii) Triamcinolone 5 mg/mL (mixed with lignocaine 1%), (repeated every 6 weeks) (iv) 0.1 mg daily (v) 1 mg daily	(i) 15 y (ii) 5 y (iii) 4 sessions (iv) NA (v) NA	Hair loss stabilization	(i) Worsened (ii) Worsened (iii) Worsened (iv) Improved (v) Improved	3 y
Gerkowicz et al. [53]/ clinical trial	16 (f)/65 y	FFA (yes)/6 y	(i) LEDs (light-emitting diodes) (for eyebrow area)	(i) Once a week (for 10 sessions) (dose per session: 37 J/cm^2, light power density: 68 mW/cm^2. The distance from the eyebrow was 15 cm. Each session lasted 9 min and 4 s)	—	Regrowth of eyebrow hair	Improved (significant increase of total eyebrow hair count)	6 m
Subash et al. [54]/ clinical trial	5 (f)/54 y	FFA (yes)/6 m<	(i) 1064 nm wavelength Nd: YAG (neodymium-doped yttrium aluminum garnet) nonablative laser	(i) 3 laser treatments (once monthly) at 14 J/cm^2, spot size 5 mm, pulse duration 3 ms at 7 Hz for 7000 to 8000 pulses (30 minutes each), 2 cm distance Using a nonablative, noncontact 1064 nm laser	—	Improvement of disease symptoms	Improved	NA

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Liu et al. [55]/case report	1 (f)/44 y	FFA (yes)/3 y	(i) HCQ (ii) Topical fluocinonide 0.05% cream (iii) Tacrolimus 0.1% ointment (iv) Hair transplantation (follicular unit extraction method) at the fronto-temporal hairline	(i) 400 mg/day (ii) NA (iii) NA (iv) 360 follicular units (FU; 630 hairs) (after 2 years of disease stabilization)	1.5 m	Improvement of disease symptoms and growth and survival of transplanted hair follicles	Improved (significant hair growth during 4 years of f/u)	4 y
Trüeb et al. [56]/case report	1 (f)/57 y	FFA (yes)/9 y	(i) Topical pimecrolimus 1% b.i.d (ii) Intralesional triamcinolone acetonide (iii) Autologous hair transplantation (follicular unit extraction method) at the frontal hairline	NA	—	Improvement of disease symptoms and growth and survival of transplanted hair follicles	Improved (significant hair growth at 2nd year of f/u)	2 y
Audickaite et al. [57]/ case series	10 (f: 9, m: 1)/ 28–58 y	FFA (yes)/2–10 y	(i) Hair transplantation (follicular unit extraction method or strip technique) at the eyebrow area	(i) 120 to 270 single hair follicles per eyebrow	—	Growth and survival of transplanted hair follicles	Worsened (8 pts achieved significant hair growth at year 1&2 of f/u; however, 3 of 4 pts with 4 years of f/u began to lose the transplanted hair follicles)	4 y
Vañó-Galván et al. [58]/retrospective review	51 (f: 48, m: 3)/54 y	FFA (yes)/NA	(i) Hair transplantation (follicular unit extraction method: $n = 7$, strip technique: $n = 44$) at the frontal hairline ($n = 22$), temporal hairline ($n = 30$) and eyebrow area ($n = 15$)	(i) 1345 single hair follicles per surgical procedure (after 15 months of disease stabilization)	—	Growth and survival of transplanted hair follicles	Worsened (mean rate of survived transplanted follicles at 1, 2, 3, and 5 years of f/u was 87%, 71%, 60%, and 41%, respectively)	3.2 y

Table 1: Continued.

Author/type of study	NR of PTs (gender)/ mean age of PTs	DX (HISTOLOGY)/ mean of disease duration	Therapeutic regimen			Outcome measurement	Overall response to treatment (improved, stabilized, worsened)	Follow-up duration
			Agent (number or percent of administered patients)	Dose	Duration			
Jiménez and Poblet [59]/case series	3 (f)/70 y	FFA (yes)/10.6 y	(i) Hair transplantation	(i) 20 to 80 single hair follicles per surgical procedure (after disease stabilization)	—	Growth and survival of transplanted hair follicles	Worsened (1 year after transplantation, significant hair growth was seen (90%<), but in the 4th year of f/u, less than 30% of transplanted hair follicles survived)	4.7 y

Table 2: The efficacy of treatment modalities hired for FFA treatment.

Treatment modality (number of administered patients)	Monotherapy			Combination therapy (with other treatment modalities)		
	Improved	Stabilized	Worsened	Improved	Stabilized	Worsened
ITAIs ($n = 287$)	45 (16%)	106 (37%)	14 (5%)	33 (11%)	71 (25%)	18 (6%)
Oral corticosteroids (prednisone) ($n = 6$)	—	—	1 (17%)	—	—	5 (83%)
5-alpha-reductase inhibitors (finasteride/dutasteride) ($n = 508$)	77 (15%)	78 (15%)	9 (2%)	18 (4%)	250 (49%)	76 (15%)
Oral isotretinoin/alitretinoin ($n = 38$)	13 (34%)	—	3 (8%)	22 (58%)	—	—
HCQ ($n = 256$)	25 (10%)	37 (15%)	26 (10%)	32 (12%)	85 (33%)	51 (20%)
Topical minoxidil 5% ($n = 101$)	7 (7%)	—	—	13 (13%)	72 (71%)	9 (9%)
Doxycycline ($n = 20$)	2 (10%)	—	2 (10%)	7 (35%)	—	9 (45%)
Topical corticosteroids ($n = 312$)	1 (0.3%)	—	—	82 (26%)	117 (37.5%)	112 (35.2%)
Topical tacrolimus/pimecrolimus ($n = 140$)	—	—	—	84 (60%)	52 (37%)	4 (3%)
Topical retinoids ($n = 9$)	—	—	—	3 (33%)	6 (67%)	—
Oral minoxidil ($n = 8$)	7 (87.5%)	—	—	1 (12.5%)	—	—
Methotrexate ($n = 4$)	—	2 (50%)	2 (50%)	—	—	—
PRP ($n = 8$)	1 (12.5%)	—	—	7 (87.5%)	—	—
Tildrakizumab ($n = 1$)	—	—	—	1 (100%)	—	—
Intramuscular steroids ($n = 18$)	—	—	—	15 (83%)	—	3 (17%)
LED ($n = 16$)	16 (100%)	—	—	—	—	—
Nd:YAG nonablative laser ($n = 5$)	5 (100%)	—	—	—	—	—
Hair transplantation ($n = 60$)	1 (2%)	—	57 (95%)	2 (3%)	—	—
Topical bimatoprost ophthalmic solution 0.03% ($n = 4$)	1 (25%)	—	—	3 (75%)	—	—

other medications; most often with topical treatments (topical steroids, topical minoxidil, topical retinoids, topical tacrolimus or pimecrolimus) or intralesional corticosteroids), of which, about 47% with monotherapy and 5% with combination therapy reported improvement, and 48% with monotherapy and 73% with combination therapy reported stabilization of the disease status after a course of 6–18 months of treatment.

Topical corticosteroids were the second prevalent medication used in FFA patients (312 patients); however, they were always utilized in combination with other treatment modalities and made it difficult to evaluate their effectiveness individually.

Systemic corticosteroids seem to be ineffective in improving FFA progression. All the 6 cases treated with oral corticosteroids as monotherapy or combination therapy experienced worsening of the disease status, as well as the patients taking intramuscular triamcinolone acetonide.

Intralesional corticosteroid injection was reported as one of the most effective treatments; 27% with monotherapy and 27% with combination therapy reported improvement, and 64% with monotherapy and 58% with combination therapy reported stabilization of the disease status.

Although topical calcineurin inhibitors (tacrolimus/pimecrolimus) were always prescribed with other treatment modalities as combination therapy, satisfactory results were reported (60% improved and 37% stabilized).

Improvement was reported in 28% and 19% of the patients taking oral antimalarial drugs (hydroxychloroquine/chloroquine) as monotherapy and combination therapy, respectively, as well as stabilization in 37% and 51% of the mentioned patients.

Oral isotretinoin (or alitretinoin) had the most effect on improving the facial papules of FFA patients, with a 92% rate of facial papule improvement.

Low-dose oral minoxidil was prescribed only once in the literature for the purpose of eyebrow regrowth in 7 patients [22]. The results were satisfactory, as complete regrowth in 2 patients and partial regrowth in 5 patients were achieved. Moreover, topical bimatoprost ophthalmic solution 0.03% was reported as a hopeful medication for eyebrows regrowth in FFA patients [27, 35]; as well as light-emitting diodes (LEDs) therapy [53].

Also, using the Nd:YAG nonablative laser was reported as an effective method to improve disease symptoms [54].

Platelet-rich plasma (PRP) injection was hired to achieve stabilization of hair loss and improvement of hairline recession in 8 FFA patients, which showed noticeable positive results [28, 29].

Tildrakizumab (interleukin-23 monoclonal antibody) was administered to a recalcitrant FFA patient who had not responded to various topical and systemic medications; however, symptomatic improvement at week 16 and objective clinical and dermoscopic improvement at week 28 were observed with no adverse effects [31].

FFA patients who hired the hair transplantation technique achieved complete satisfaction; however, the result was temporary. Most of the transplanted hair follicles did not survive 2–4 years after transplantation.

4. Discussion

As no definitive therapeutic regimen is specified for FFA, we searched the literature for utilized FFA treatments and their effects.

Currently, no standardized criteria are identified to evaluate the treatment efficacy in FFA patients.

Recently, some authors used the LPPAI (Lichen Planopilaris Activity Index), which is calculated by assessing

subjective symptoms (pruritus, burning, and pain) and objective signs (erythema, perifollicular scaling, and hair loss) of the disease [42, 43]. Authors hiring other criteria than LPPAI mainly focus on the improvement of hair loss by various methods like counting hair shafts, serial photographical evaluation, or assessing the frontotemporal hair line resection according to the patient reports (represented in Table 1).

As the main complaint of FFA patients is permanent hair loss [1], we propose that improvement or stabilization of hair loss should be considered for outcome measurement of FFA treatment.

In our review, intralesional corticosteroid injection and 5-alpha-reductase inhibitors (finasteride/dutasteride) were reported as the most effective treatment modalities, according to the disease improvement or stabilization rate. Some authors have revealed the accompanying role of androgenetic alopecia in FFA [45]. Perhaps, it might be an explanation for antiandrogenic drugs' efficacy.

Oral isotretinoin (or alitretinoin) is considered as the most promising treatment for improving facial papules in the context of FFA; however, it had minimal effects on hair regrowth or stabilization of hairline recession in FFA patients.

Also, topical calcineurin inhibitors (tacrolimus/pimecrolimus) can be considered a useful adjuvant treatment in combination therapies.

Oral antimalarial drugs (hydroxychloroquine/chloroquine) cannot be proposed to FFA patients as a hopeful and effective treatment, according to the low rate of disease improvement or stabilization with either monotherapy or combination therapy; neither can topical corticosteroids be recommended.

Tildrakizumab, oral minoxidil, topical bimatoprost ophthalmic solution 0.03%, LED therapy, Nd: YAG nonablative laser therapy, and PRP injection are newly introduced therapeutic methods for FFA and have shown satisfactory results. They can be administered cautiously for FFA patients with progressive disease status despite taking standard medications; however, more clinical trials and investigations are needed to prove their effectiveness and propose them as promising treatments for FFA.

Although hair transplantation results are satisfactory in the first 2 years, the long-term outcome is disappointing.

We propose hair transplantation for FFA patients with at least 2 years of disease stabilization. The donor region should be observed carefully in terms of follicular inflammation. Also, close postoperative follow-up sessions are highly recommended (every 4–6 months). In case of existence of any sign of perifollicular hyperkeratosis or erythema after the transplantation, medical treatment must be prescribed. These patients should be followed up for a long time.

Finally, a complete justificatory discussion should be conducted with the patients in terms of the duration of the results and the risk of hair loss in the long term follow-up.

Limitations of this study were the various doses and durations of therapeutic regimens with different follow-up periods and different scales to assess treatment outcome, which made it difficult to evaluate the true efficacy of medications.

5. Conclusion

Intralesional corticosteroid injection and 5-alpha-reductase inhibitors (finasteride/dutasteride) were reported as the most effective treatment modalities. Oral isotretinoin (or alitretinoin) is considered the most promising treatment for improving facial papules in the context of FFA; however, it had minimal effects on hair regrowth or stabilization of hairline recession in FFA patients. Also, topical calcineurin inhibitors (tacrolimus/pimecrolimus) can be considered as a useful adjuvant treatment in combination therapies. Oral antimalarial drugs (hydroxychloroquine/chloroquine) cannot be proposed to FFA patients as a hopeful and effective treatment. Tildrakizumab, oral minoxidil, topical bimatoprost ophthalmic solution 0.03%, LED therapy, Nd: YAG nonablative laser therapy, and PRP injection are newly introduced therapeutic methods for FFA and have shown satisfactory results. They can be administered cautiously for FFA patients with progressive disease status despite taking standard medications. Although hair transplantation results are satisfactory in the first 2 years, the long-term outcome is disappointing.

Data Availability

The data are available on request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

A.M.B. performed the research. M.G. and G.R.R. designed the research study. A.M.B. and T.G. contributed essential reagents or tools. A.M.B. and B.G. wrote the paper. G.R.R., M.G., and A.P. revised the paper.

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