Novel Treatment Approaches for Central Centrifugal Cicatricial Alopecia: A Comprehensive Literature Review

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ABSTRACT

Central centrifugal cicatricial alopecia (CCCA) represents the most common form of scarring alopecia in African American women, affecting approximately 15% of this population. While conventional treatments including topical corticosteroids and intralesional injections remain first-line therapies, recent years have witnessed the emergence of novel therapeutic approaches that show promise in addressing the underlying pathophysiology of this challenging condition.

OBJECTIVE:

To comprehensively review and analyze novel treatment modalities for CCCA introduced within the last 5-10 years, with more emphasis on pharmacologic, procedural, laser, and regenerative therapies.

LINK TO MANUSCRIPT:

METHOD

A comprehensive literature review was conducted focusing on studies published between 2015-2024, including systematic reviews, clinical trials, case series, and case reports describing novel treatments for CCCA.

EMERGING THERAPEUTIC TARGETS

Systematic reviews have identified TNF inhibitors, particularly adalimumab and infliximab, as potential agents in scarring alopecias.[20] A comprehensive systematic review by researchers examining JAK and TNF inhibitors found that adalimumab induced rapid and stable improvement in most patients with rare, tolerable adverse effects. However, paradoxical cicatricial alopecia has been reported with some TNF inhibitors, thus necessitating careful patient selection.[20] Dupilumab, an IL-4/IL-13 inhibitor, remains unstudied in CCCA but may have mechanistic relevance given type 2 inflammatory involvement. [21]

Hydroxychloroquine may be utilized in related cicatricial alopecias, with particular efficacy shown in treating lichen planopilaris and frontal fibrosing alopecia.[22] While specific data for CCCA is limited, the anti-inflammatory and immunomodulatory properties of antimalarials make them potentially useful in CCCA management.[22,23]

Apremilast, an oral PDE4 inhibitor approved for psoriasis, is under investigation for CCCA (NCT03521687) based on its suppression of pro-inflammatory cytokines.[24] Early pilot studies initiated in 2018 remain unpublished. Azelaic acid is also being investigated in scarring alopecias for anti-inflammatory/anti-proliferative effects (NCT05416333), though data is still limited.[25, 26]

An ongoing interventional study at Wake Forest University aims to compare outcomes between topical steroid plus oral antibiotic group, and topical minoxidil topical steroid plus intralesional steroid group and topical minoxidil in patients diagnosed with CCCA. Results are likely to be reported in early 2026.[27]

RESULTS

Emerging treatments include antifibrotic agents (oral and topical metformin), targeted immunomodulators (JAK inhibitors), botanical formulations, PDE4 inhibitors, regenerative therapies (platelet-rich plasma [PRP], low-level light therapy [LLLT]), and surgical/procedural approaches. Case series and mechanistic studies document symptomatic relief, halting of progression, and, in some cases, hair regrowth.

Treatment Modality	Number of studies	N	Outcome
Oral Metformin	1 retrospective case series	12	Significant symptomatic improvement in nine out of twelve patients (including scalp pain, pruritus, and inflammation). 50% (6/12) demonstrated clinical evidence of hair regrowth after at least six months of treatment.
Topical Metformin	1 case report	2	Substantial hair regrowth after 4-6 months of treatment.
Botanical formulation (turmeric (curcumin), fenugreek oil, and Fo-ti)	1 pilot clinical trial	8	Cessation of scalp itching within two weeks and visible hair regrowth within two months, sustained over six months of treatment.
PRP* therapy	2 case reports	2	Restoration of normal follicular density along the temporal hairline with greater than 50% improvement in hair density along the scalp vertex in one patient, but reduced follicular density 6 months after treatment cessation
LLLT**	1 prospective study	4	Increased hair density in three out of four patients

*Platelet-rich Plasma
**Low-Level Light Therapy

DISCUSSION

In summary: time is hair. Early treatment initiation of CCCA may preserve hair follicles that have not fully succumbed to fibrosis, which potentially allows for increased follicular density and regrowth in areas previously thought to represent end-stage scarring. Most successful outcomes appear to result from combination approaches targeting multiple pathogenic pathways simultaneously. The integration of anti-inflammatory, antifibrotic, and regenerative modalities may offer superior outcomes compared to monotherapy. Several treatments, particularly PRP and topical therapies, require ongoing maintenance to sustain benefits; perhaps CCCA may be better conceptualized as a chronic condition requiring long-term management rather than a curable disease.

CONCLUSION

The treatment landscape for CCCA has undergone significant transformation in recent years, with novel therapeutic approaches offering hope for patients with this challenging condition. The emergence of antifibrotic agents like metformin, targeted immunomodulators such as JAK inhibitors, and regenerative therapies including PRP and LLLT represents a paradigm shift from purely anti-inflammatory approaches to treatments that address the underlying fibrotic and regenerative aspects of the disease.

While these developments are encouraging, the evidence base still remains limited by small sample sizes and short follow-up periods. The establishment of treatment guidelines through expert consensus illustrates a vital step forward, but larger, well-designed randomized clinical trials are necessary to establish further evidence-based treatment protocols. Biomarker development may be prioritized to better predict treatment responses and guide therapy selection.
As our understanding of CCCA pathophysiology continues to evolve, the integration of novel therapeutic modalities with traditional treatments offers the potential for significantly improved outcomes for patients affected by this condition.