

Treatment for central centrifugal cicatricial alopecia—Delphi consensus recommendations



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Background: There is no established standard of care for treating central centrifugal cicatricial alopecia (CCCA), and treatment approaches vary widely.

Objective: To develop consensus statements regarding the use of various pharmacological therapies in treating adults with CCCA.

Methods: We invited 27 dermatologists with expertise in hair and scalp disorders to participate in a 3-round modified Delphi study between January and March 2023. Statements met strong consensus if 75% of respondents agreed or disagreed. Statements met moderate consensus if 55% or more but less than 75% agreed or disagreed.

Results: In round 1, 5 of 33 (15.2%) statements met strong consensus, followed by 9 of 28 (32.1%) in round 2. After the final round 3 meeting, strong consensus was reached for 20 of 70 (28.6%) overall statements. Two statements achieved moderate consensus.

Limitations: This study included only English-speaking, US-based dermatologists and did not consider nonpharmacological therapies.

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Conclusion: Despite varying opinions among dermatologists, consensus was reached for several statements to help clinicians manage CCCA. We also highlight areas that lack expert consensus with the goal of advancing research and therapeutic options for CCCA. (J Am Acad Dermatol 2024;90:1182-9.)

Key words: alopecia; CCCA; central centrifugal cicatricial alopecia; cicatricial alopecia; consensus; delphi; dermatology; guidelines; hair loss; modified delphi; recommendation; scarring alopecia; therapy; treatment.

INTRODUCTION

Central centrifugal cicatricial alopecia (CCCA) is a primary scarring alopecia that predominantly affects women of African descent.¹ The etiology of the disorder is currently unknown; however it is likely multifactorial, involving an interplay of genetic, behavioral, and environmental factors.¹ Multiple studies have documented the impaired quality of life associated with CCCA, highlighting the burden of disease.^{2,3} To date, no randomized controlled trials have investigated therapies for CCCA. The current literature comprises case reports, small case series, and single center case-control studies with few evidence-based treatment recommendations.⁴⁻¹¹ It is widely accepted that diagnosis and treatment should be prompt as CCCA is a “trichologic emergency,” meaning immediate action is required to prevent irreversible hair follicle damage.¹² Treatment for the disorder is largely guided by clinical judgment, contributing to the wide variability in treatment approaches. We aimed to develop treatment recommendations for CCCA in adults to address these management gaps.

The Delphi process is a validated group communication method used to determine core outcomes, diagnostic evaluation, and treatment recommendations.^{13,14} The primary goal of a Delphi is to achieve group convergence of opinion through an ordered process with key components of anonymity, controlled feedback, and iterative rounds.^{15,16} The process of obtaining experts' opinions is most useful when there is lack of evidence within a specific area. The modified version of the Delphi, previously described, involved a steering committee which facilitated the group communication process and vetted the long list of potential therapies.¹⁷ In principle, these modifications allow for statement clarification and structure effective and faster consensus.

CAPSULE SUMMARY

- Robust research on central centrifugal cicatricial alopecia therapy is limited, and no established guidelines exist for treating this common hair disorder.
- This consensus evaluates appropriate therapies for central centrifugal cicatricial alopecia and establishes a framework to guide clinical practice.

Based on these considerations, we determined the modified Delphi process as a feasible method of developing consensus statements for CCCA management.

Disease activity and severity may influence therapeutic choice in CCCA. For example, the disorder has 2 main stages: early (inflammatory) and late (scarring).¹ Antiinflammatory therapies appropriately target the early

disease stage, while efforts to promote hair regrowth are more apparent once the primary inflammatory process is controlled. We offer recommendations specific to disease stage in these statements.

METHODS

Participant selection

A steering committee of 3 dermatologists (S. T., C. F., P. A.) recruited US-board certified dermatologists with recognized expertise in hair and scalp disorders and who actively manage adult patients with CCCA.

Delphi questionnaire and consensus threshold

This was a 3-round Delphi process between January and March 2023, with 2 surveys facilitated by a web-based software (DelphiManager) and a final in-person meeting. A detailed literature search in PubMed, Embase, Cochrane Library, and Scopus was conducted to develop a list of evidence-based pharmacological options for CCCA. This list formed the basis of the round 1 survey, which the steering committee designed. The steering committee also guided executive decisions throughout the study. However, they were excluded from voting.

For each Delphi round, experts indicated how much they agreed with a statement using a numerical score from 1 to 9 or unable to rate. The following scoring scale was used for data analysis: 1 to 3 corresponded to do not agree with statement; 4 to 6 somewhat agree with statement; and 7 to 9 very

Abbreviation used:

CCCA: central centrifugal cicatricial alopecia

much agree with statement. Consensus threshold values largely vary among Delphi studies.^{13,14,17-19} We set the consensus threshold to greater than or equal to 75% to represent strong consensus. Therefore, statements met strong consensus if 75% or more of respondents rated it 1 to 3 (consensus disagreement) or 7 to 9 (consensus agreement). Statements met moderate consensus if at least 55%, but less than 75%, of respondents agreed or disagreed.

The survey organized statements into 5 categories: topical, systemic, procedural, supplements, and behavioral. Statements that met strong consensus in a round were omitted from subsequent rounds. Statements not meeting strong consensus in round 1 were removed or modified according to participant feedback and redistributed to the participants. Statements presented for rating in round 2 also included new statements proposed by respondents. In round 3, experts reviewed all statements that achieved strong and moderate (at least 55% but less than 75%) consensus to form the final recommendations. For statements that included the terms “active” or “high-potency topical corticosteroids,” a help text was provided to clarify “active” as symptomatic or progressing and “high-potency topical corticosteroids” as class 1 or 2.

RESULTS

Of the 27 invited dermatologists, 21 (78%) enrolled and completed round 1; 20 (74%) completed round 2; and 16 (59%) completed round 3, 13 via in-person discussion at the 2023 American Academy of Dermatology Annual Meeting and 3 online. Participants were located across 12 US states, with 71%, 29%, and 0% reporting urban, suburban, and rural settings, respectively. Most participants (71%) practiced in academic institutions while 29% worked primarily in private practice. On average, the dermatologists reported treating 52 (SD = 56) patients with CCCA monthly and had 18.8 (SD = 11.3) years of experience managing adults with CCCA.

Supplementary Fig 1, available via Mendeley at <https://doi.org/10.17632/4wph4b4bbw.1> outlines the steps of this Delphi study. Strong consensus was achieved for 20 statements (28.6%): 5 after round 1, 9 after round 2, and 6 after round 3. Tables I-V displays the 20 statements separated by category. Please see Supplementary Tables I-III, available via Mendeley at

<https://doi.org/10.17632/4wph4b4bbw.1> to view all treatments evaluated by experts in each round. All but 7 statements addressed pharmacological therapies (ie, utility, administration route, dosage, frequency). The remaining 7 statements addressed the following topics: screening recommendations (3), hair care (2), and best practices for hair transplantation (2). The greatest consensus was reached for guidance of procedural treatment (47%) followed by guidance of systemic treatments (33%). The category with the least consensus was supplements.

Topical

There were 18 total statements regarding topical corticosteroids, minoxidil, calcineurin inhibitors, compounded metformin cream, and medicated shampoos. The group established consensus for high-potency topical corticosteroids as first-line topical therapy and provided a utility regimen during initial and maintenance treatment (Table I). There was a divergence of thought for questions about topical minoxidil, with many respondents reporting use of low-dose oral minoxidil as an alternative to topical minoxidil. One statement regarding the use of topical and/or low-dose oral minoxidil as adjunct therapy achieved strong consensus (Table I). Recommendations for topical calcineurin inhibitors, compounded metformin cream, and medicated shampoos did not reach consensus.

Systemic

Of 15 total questions regarding systemic therapies, 5 met strong consensus, and the systemic category included the only 2 statements that achieved consensus disagreement. To establish an appropriate treatment duration with oral tetracyclines, we proposed the options of 200 mg doxycycline per day up to 3 or 6 months to the experts. However, both options reached strong consensus agreement after round 2. After clarification during the Round 3 discussion, 200 mg doxycycline per day up to 6 months met strong consensus agreement, with the emphasis that the doxycycline dose could be lowered or discontinued earlier if the patient's symptoms and hair loss stabilize. When given the choice of 3 months or 6 months of doxycycline 200 mg daily, the group favored up to 6 months of therapy, and therefore the option of up to 3 months met strong consensus disagreement (Table II). Experts also strongly disagreed with using systemic corticosteroids for treating CCCA. The utility of oral spironolactone and immunosuppressants such as mycophenolate mofetil, Janus kinase inhibitors, cyclosporine, and methotrexate did not achieve consensus.

Table I. Delphi consensus recommendations for the treatment of CCCA in adults—topical

Statements meeting strong consensus ($\geq 75\%$)	<i>n</i>	Delphi round for consensus
High-potency topical corticosteroids can be prescribed as first-line topical treatment (alone or in combination) to treat CCCA.	20/21	1
A high-potency topical corticosteroid would be appropriate if applied to the scalp (alone or in combination) daily for at least 4 wk and then tapered to a maintenance dose.	16/20	2
A high-potency topical corticosteroid should be applied to the scalp (alone or in combination) as a maintenance dose for 2-5 times weekly.	17/21	1
Topical minoxidil 5% or greater or oral minoxidil would be appropriate as adjunct treatment in adults with CCCA.*	15/16	3

CCCA, Central centrifugal cicatricial alopecia.

*Statement combines 2 therapeutic categories: topical, oral.

Table II. Delphi consensus recommendations for the treatment of CCCA in adults—systemic

Statements meeting strong consensus ($\geq 75\%$)	<i>n</i>	Delphi round for consensus
Oral doxycycline (or other tetracycline antibiotics) up to 200 mg per d is appropriate (alone or in combination) up to 3 mo in the treatment of adults with active CCCA. (CONSENSUS DISAGREEMENT)*,†	14/16	3
Oral doxycycline (or other tetracycline antibiotics) up to 200 mg per d is appropriate (alone or in combination) up to 6 mo in the treatment of adults with active CCCA.	15/20	2
Oral antibiotics are appropriate (alone or in combination) for treatment of adults with active CCCA.	16/20	2
Systemic corticosteroids are appropriate for treatment of active CCCA in adults. (CONSENSUS DISAGREEMENT)†	14/16	3

CCCA, Central centrifugal cicatricial alopecia.

*Statement met strong consensus agreement in round 2 but changed to strong consensus disagreement after clarification and group discussion in round 3.

†CONSENSUS DISAGREEMENT = strong consensus disagreement.

Procedural

The group established strong consensus for intralesional triamcinolone acetonide 5 to 10 mg/cc as appropriate for the active and maintenance treatment of CCCA, with a 20 mg maximum dose per session regardless of disease stage (Table III). However, consensus was not reached for the frequency of intralesional corticosteroids during maintenance. Experts overwhelmingly agreed hair transplantation was not appropriate in the setting of active inflammation, and the disease should be stable for at least 1 year prior to the procedure. Statements for platelet rich plasma/fibrin matrix did not reach consensus as the group agreed there was limited information to support its use for CCCA.

Supplements

Strong consensus was achieved for 2 of 10 questions addressing supplements (Table IV). Consensus was not reached on any statements relating to zinc or antioxidant/anti-inflammatory/antiandrogenic supplements.

Behavioral

Three behavioral statements met strong consensus (Table V). Statements regarding the use of high thermal heat hair practices and permanent hair dye did not meet consensus. Additionally, a statement about screening CCCA patients for type 2 diabetes mellitus did not reach consensus. Guidance regarding screening for anxiety and depression did not reach consensus. However, experts did agree that it was important to ask about alopecia related quality of life.

Moderate consensus

The use of hydroxychloroquine and guidelines for chemical hair relaxers/straighteners were considerably divergent. The group discussed concerns for monitoring labs and mono vs combination therapy with hydroxychloroquine. Nonetheless, hydroxychloroquine may be appropriate for a subset of patients with inadequate response to other therapies or those who cannot tolerate oral antibiotics. Recommendations to avoid hair care practices that cause inflammation were favored, but specific

Table III. Delphi consensus recommendations for the treatment of CCCA in adults—procedural

Statements meeting strong consensus ($\geq 75\%$)	n	Delphi round for consensus
Intralesional triamcinolone acetonide 5-10 mg/cc administered every 4-12 wk should be prescribed (alone or in combination) for treatment of adults with active CCCA.	18/21	1
Intralesional triamcinolone acetonide 5-10 mg/cc may be used (alone or in combination) as maintenance therapy for adults with CCCA.*	16/20	2
It is appropriate to limit the maximum dose of intralesional triamcinolone acetonide administered in 1 session to minimize systemic absorption.	17/20	2
The maximum dose of intralesional triamcinolone acetonide administered in 1 session to an adult with CCCA is up to 20 mg. [†]	15/16	3
Hair transplantation should be avoided in patients with CCCA who have evidence of active scalp inflammation.	20/21	1
Hair transplantation may improve cosmesis for patients with CCCA without evidence of active scalp inflammation for at least 1 y.	14/16	3
There is limited information to support the use of platelet rich plasma/fibrin matrix as treatment for CCCA. [‡]	14/16	3

CCCA, Central centrifugal cicatricial alopecia.

*Statement met strong consensus agreement in round 2, but experts voted in round 3 to add dose of 5 to 10 mg/cc.

[†]New statement added and voted on in round 3.

[‡]Experts voted to replace "inadequate" with "limited" in round 3.

Table IV. Delphi consensus recommendations for the treatment of CCCA in adults—supplements

Statements meeting strong consensus ($\geq 75\%$)	n	Delphi round for consensus
It is appropriate to screen patients with CCCA for serum nutritional deficits of vitamin D. Deficit correction with oral supplements is appropriate.	16/20	2
It is appropriate to screen patients with CCCA for serum nutritional deficits of iron/ferritin. Deficit correction with oral supplements is appropriate.	15/20	2

CCCA, Central centrifugal cicatricial alopecia.

practices were not indicated. After round 3, the participants agreed to include the following recommendations with moderate consensus agreement:

- Oral hydroxychloroquine is appropriate treatment (alone or in combination) for active CCCA in patients with inadequate response to other therapies. ($n = 13/20$).
- It is important to discuss discontinuing or limiting the use of chemical hair relaxers and straighteners in patients with CCCA ($n = 13/20$).

DISCUSSION

In this Delphi consensus study, dermatologists with hair and scalp expertise formed 20 consensus statements for treating CCCA in adults. The group agreed strongly on recommendations for topical and intralesional corticosteroids, oral antibiotics, topical and/or low-dose oral minoxidil, and hair transplantation, while recommendations for oral hydroxychloroquine only reached moderate consensus agreement. The group reached a strong consensus disagreement for

the utility of systemic corticosteroids. There was a lack of consensus for other therapies such as topical calcineurin inhibitors, topical metformin, and oral hair growth supplements.

Treatment recommendations were presented with respect to disease activity, and some signs and symptoms of early scalp inflammation seen in CCCA include pruritus, tenderness, and hair breakage.¹ However, choice of therapy may be influenced by other factors such as prior therapeutic response, comorbidities, and health insurance.^{1,20} The data supporting the use of the pharmacological agents discussed are limited. Many anti-inflammatory agents halt disease progression or provide symptomatic relief but may not meet patient expectations of hair regrowth.¹ Thus, a patient-centered discussion about the therapeutic goals and plan are paramount.

Experts also highlighted nuances to treatment approach, for example the option to lower the 6-month course of doxycycline 200 mg daily to 40 to 50 mg daily after 3 months if the patient's

Table V. Delphi consensus recommendations for the treatment of CCCA in adults—behavioral

Statements meeting strong consensus ($\geq 75\%$)	n	Delphi round for consensus
It is appropriate to assess how much a patient with CCCA is bothered by their hair loss and if appropriate, refer for counseling or support groups.*	17/20	2
Therapy for CCCA includes discontinuing or limiting traction inducing hairstyles if possible.	18/21	1
The recommended frequency of scalp shampooing in adult patients with CCCA is at least once every 2 wk. [†]	14/16	3

CCCA, Central centrifugal cicatricial alopecia.

*Statement met strong consensus agreement in round 2, but experts voted in round 3 to add “or support groups.”

[†]New statement added and voted on in round 3.

symptoms and hair loss stabilize as submicrobial dosing is optimal for antibiotic stewardship. Clinicians can discontinue the doxycycline early if patients become asymptomatic with no signs of inflammation. Though not included in the consensus statements, these considerations are important.

The published evidence for supplements and behavioral practices specific to CCCA are meager; however, the experts shared unique insights. In round 3, experts voted to add a new recommendation: frequency of scalp shampooing at least once every 2 weeks. The group did not converge on a specific shampoo, but clinicians should develop a list of preferred products and consider shampoos with vehicles that are more tolerable for coily/curly hair (ie, cause less dryness and resulting hair breakage).

Traction-inducing hairstyles (eg, tight ponytails, hair braiding) may flare CCCA and should be minimized. The discussion regarding hairstyles should be guided by cultural sensitivity, focusing on healthy hair care practices (eg, increasing time with natural hair between styles) and alternative low-tension styles as opposed to what the patient should avoid.^{21,22} Hair and scalp experts often screen and correct serum vitamin deficiencies in alopecia patients to promote a healthy environment for hair growth.²³ Our group specified screening for serum vitamin D and iron/ferritin levels, which is supported in Black women who are at high risk of these mineral deficiencies.²⁴⁻²⁷

Importantly, consensus does not represent whole group agreement but rather reflects the array of expert opinions and the limited high-quality evidence available to inform the treatment of CCCA. Hence, there is a critical need for robust research and investigations focused on the etiology and effective interventions for CCCA. Nevertheless, these recommendations serve as a framework, particularly for clinicians who are inexperienced in managing CCCA.

This study has notable limitations. Most study participants completed all questionnaires; however,

1 expert missed the deadline to complete the round 2 questionnaire and was excluded from voting in subsequent rounds. Another 4 participants were unable to attend the round 3 meeting, possibly introducing attrition bias. The questionnaire did not consider nonpharmacological therapies for CCCA. Treatment options not elucidated during the literature search or the expert panel were also not included in the voting process. Therefore, recommendations for use of finasteride/dutasteride, biotin supplements, microneedling, hydradermabrasion, or light therapies for CCCA were not provided. The questionnaire also did not include treatment considerations for specific patient populations (eg, pediatric, pregnant, breastfeeding).

Participant feedback revealed variable interpretations of select questions; clarification was provided to those who attended the round 3 meeting before votes were cast. Several statements indicate treatments can be used “alone or in combination” without providing decision-making instructions. Although this reflects the diversity of options, combination therapy is typically perceived as superior to monotherapy for CCCA.¹ Despite incorporating procedures to minimize bias (ie, rounds chaired by the nonvoting steering committee, regular reminders of anonymity to the group), the round 3 in-person discussion was limited by time and may have introduced normative pressure from other group members due to loss of anonymity. Importantly, we recognize this consensus document does not include feedback or experiences from patient representatives, a key stakeholder group involved in guiding therapy for CCCA. Furthermore, nonrandom sampling of experts and the exclusion of nondermatologists may have introduced sampling bias.

CONCLUSION

Despite diversity in expert opinion, these consensus recommendations outline multiple treatment options for CCCA, thereby extending hope to patients and reducing the burden of disease. We call for increased

research efforts to understand the etiology, comorbidities, and treatment efficacy of CCCA. Furthermore, we advocate for randomized placebo-controlled trials for safety and efficacy of therapeutic agents for CCCA.

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Conflicts of interest

Dr Barbosa has served as a consultant or advisory board member to the following companies in the last 2 years: Eli Lilly, Pfizer, UCB, and Vichy. Dr Harvey has served as a consultant or advisory board member for Eli Lilly, Skinceuticals, Janssen, L'Oréal, Unilever, Pfizer, and Abbvie. Dr Mayo has served as an investigator or consultant for Arcutis, Acelyrin, BMS, ChemoCentryx, Eli Lilly, Galderma, Janssen, Leo Pharma, Novartis, Pfizer, and Procter & Gamble. Dr McMichael has grants/research or consulting relationships with Concert, Procter & Gamble, Incyte, Eli Lilly, Janssen, Pfizer, Arcutis, Almirall, AbbVie, Galderma, Bristol Myers Squibb, Sanofi-Genzyme, UCB, Revian, Johnson & Johnson, L'oreal, and Leo. Dr Piliang has relationships with Eli Lilly and Company, Pfizer Inc, and Procter & Gamble Company. Dr Tosti is consultant for DS Laboratories, Monat Global, Almirall, Tirthy Madison, Eli Lilly, P&G, Pfizer, Myovant, Bristol Myers Squibb, Ortho Dermatologics, Curallux LLC and PI for Eli Lilly, Concert. Dr Frey has served as a consultant or advisor for the following: Procter & Gamble, Sun Pharma, Galderma, CeraVe, La Roche Posay, Regeneron, Avita, and Ferndale. Dr Adotama has served as a consultant or advisory board member for Sanofi Regeneron, Janssen, Bristol-Myers, and Argenx. Dr Taylor has served as a consultant, advisory board member, and/or speaker for AbbVie, Arcutis, Armis Scientific, Avita, Beiersdorf, Biorez, Bristol-Myers Squibb, Cara Therapeutics, Dior, Eli Lilly, EPI Health, Evolus, Galderma, GloGetter, Hugel America, Incyte, Johnson & Johnson, L'Oreal USA, MedScape, MJH LifeSciences, Pfizer, Piction Health, Sanofi, Scientis US, UCB, and Vichy Laboratoires. She has received royalties from McGraw-Hill. She has served as an investigator for Allergan, Concert Pharmaceuticals/Sun Pharma, Croma-Pharma GmbH, Eli Lilly, and Pfizer. Authors Jackson, Sow, Dinkins, Drs Aguh, Ayode, Burgess, Callender, Cotsarelis, Grimes, Kindred, Lester, Sicco, Oboite, Ogunleye, Olsen, Osei-Tutu, and Shapiro have no conflicts of interest to declare.

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