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Patch testing and contact allergen avoidance in patients with lichen planopilaris and/or frontal fibrosing alopecia: a cohort study

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Title: Patch testing and contact allergen avoidance in patients with lichen planopilaris and/or frontal fibrosing alopecia: a cohort study

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The incidence of frontal fibrosing alopecia (FFA) has increased since 1994, suggesting environmental causes in disease etiology.^{1,2} The development of FFA has been linked to a xenobiotic-processing enzyme genetic defect, but the exact etio-pathogenesis is still unknown.² Patch testing in British and Brazilian FFA patients identified five potentially relevant allergens.^{1,3} This study seeks to identify relevant allergens in FFA and/or lichen planopilaris (LPP) patients, and assess whether avoidance of relevant allergens impacts patients' alopecia symptoms and disease activity.

From January 2018 to June 2019, 42 patients with LPP/FFA were referred for patch testing from a specialty alopecia clinic. Patch testing included the North American Baseline Series, Cosmetic and Hairdresser Series, and 8 other potential allergens identified by 3 experienced contact dermatitis experts (JY, PS, DS) which included N-isopropyl-N'-phenyl-p-phenylenediamine (IPPD), methylchloroisothiazolinone/methylisothiazolinone (MCI/MI), Benzophenone-4, Avobenzone, Benzalkonium chloride, Carvone, Polysilicon 15, and Aminoazobenzene. Readings were performed at 48 and 96 hours. At least three months following patch testing, patients with relevant allergens participated in a brief survey to assess the impact of allergen avoidance. All surveyed patients were on stable LPP/FFA treatment regimens for at least 6 months prior to patch testing and remained on those treatments during the 3 months before survey administration. Allergens were deemed relevant if they were present in patients' personal care products (PCP) and had at least +1 patch testing reaction. Since gallates may be present in oils within PCP in concentrations small enough to be omitted from ingredient lists but still capable of eliciting allergic contact dermatitis, all +1 or higher reactions for these were considered relevant.⁶ Local institutional review board approval was granted for this study.

41 females and 1 male with a mean age of 61 years (range 25-81) underwent patch testing. Most were Caucasian (97.6%) with biopsy proven LPP (61.9%), FFA (26.2%), or LPP/FFA overlap (11.9%), and 76.2% had clinically relevant allergens found in cosmetic and PCP applicable to the scalp and face. As shown in Table 1, the most common relevant allergens included gallates (26.2%), linalool (19.0%), and fragrance mixes (19.0%). Linalool is a ubiquitous fragrance chemical found in many personal care products including cleansers, cosmetics, creams, lotions, and hair care products (shampoo, conditioner, leave in products such as hairspray, gel, etc).

Gallates are preservatives added to cosmetics to prevent the growth of yeast, fungi and bacteria and can be found in cleansers, cosmetics, liquids and creams.

The distribution of the number or type of relevant allergens in patients with LPP, FFA, or LPP/FAA did not differ widely (Table 2). Twenty patients were eligible at the time of survey administration to participate. Of these, 58.3% and 72.7% of surveyed patients who had scalp pruritus or erythema on initial presentation indicated that their scalp pruritus or erythema decreased, respectively, after at least 3 months of allergen avoidance.

Study patients continued clinic visit evaluations by the treating physician (MMS), who was blinded to patient survey responses. Perifollicular scalp erythema was graded from 0 (none) to 3 (confluent) for each scalp section (top, right, left, back). Review of medical records revealed after at least 3 months of allergen avoidance, 70% of patients had decreased scalp erythema on exam. No patient had signs or symptoms of worsening LPP/FFA.

Although no recent studies have been done on the prevalence of allergens in the general population in the United States, European studies report the prevalence for Fragrance mix I (FM I) and Fragrance Mix II (FM II) to be 1.8% and 1.9%, respectively.¹⁰ While the prevalence in the North American Contact Dermatitis Group (NACDG) results approach those of our cohort, the NACDG includes +/- reactions in their data, and we did not include these equivocal results in our patient dataset. Removing the +/- results from the 2015-2016 NACDG numbers brings the prevalence of FMI, FMII and MCI/MI allergy to roughly 10%, 4.8%, and 6.8%, respectively.¹² The higher prevalence of allergens in our patient cohort (14.3%, 9.5%, and 11.9% for FMI, FM II, and MCI/MI) suggests that our results may be important in the treatment and evaluation of patients with LPP and FFA. While an age and sex-matched control group for the current study is lacking, it is worthwhile to note that the NACDG patients were largely female (72%), white (82.7%), with an average age of 49 years, therefore slightly younger but otherwise approximating the current study population.

Whether allergic contact dermatitis directly contributes to the pathogenesis of LPP and/or FFA is unclear. Avoiding relevant allergens on the face and scalp, however, may reduce local inflammation in some patients, consistent with our findings suggesting disease improvement.

Further study should be undertaken to determine the role of these allergens in cicatricial alopecia development, especially as previous studies have suggested a correlation between lichenoid reactions and pigmented cosmetic allergic contact dermatitis.⁵ In the FFA population lichen planus pigmentosus has been increasingly reported to occur on the face and neck.⁶⁻⁸ Acquired dermal macular hyperpigmentation (ADMH) is a term that includes lichen planus pigmentosus and pigmented contact/cosmetic dermatitis, and in one study hair dye was shown to be the cause of these eruptions in up to 33% of patients.⁹ Future studies could help to determine if LPP and FFA represent a lichenoid type of contact allergy of the scalp.

This study is limited by the small sample size and inclusion of a non-validated, non-controlled survey. Strengths of this study include the reporting of patch testing results in US-based patients with LPP/FFA and assessment of outcome measures following allergen avoidance. Given the high prevalence of relevant contact allergens in patients with LPP/FFA, clinicians may consider recommending routine patch testing for this patient population.

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Tables

Table 1: Prevalence of common allergens

Allergen	Our cohort (n=42)	Aldoori et al ² (n=40)	Rocha et al ⁵ (n=63)	NACDG ⁶ *** (n=5590+)
Gallates [†]	26.2%			
Dodecyl gallate	16.7%			
Octyl gallate	4.8%			
Propyl gallate	4.8%			
Fragrance Mixes [†]	19.0%			
Fragrance Mix I	14.3%	10.0%	5.0%	11.3%
Fragrance Mix II	9.5%			
Linalool*	19.0%			2.3%
Ammonium persulfate	14.3%	22.5%		
Benzophenone 4	14.3%	12.5%	8.0%	7.0%
Propolis	9.5%			1.7%
MI/MCI**	11.9%	17.5%		13.4%
Benzoyl peroxide	9.5%			1.7%
Balsam of Peru	7.1%			

*Linalool includes Hydroperoxides of Linalool

**Methylisothiazolinone/Methylchloroisothiazolinone

***NACDG Data includes +/- reactions

[†]Indicates that some patients were allergic to more than one subtype

Table 2: Prevalence of allergens by cicatricial alopecia diagnosis

Allergen	LPP (n=26)	FFA (n=11)	LPP/FFA (n=5)	Total (n=42)
Positive Reaction	76.9%	81.8%	60.0%	76.2%
Gallates	14.2%	7.1%	4.9%	26.2%
Fragrance Mixes	19.2%	27.3%	0.0%	19.0%
Linalool	19.2%	18.2%	20.0%	19.0%