Regarding methodologic concerns in clinical studies on frontal fibrosing alopecia

To the Editor: We appreciate the opportunity to discuss some crucial aspects regarding clinical studies on Frontal Fibrosing Alopecia (FFA).

The pathogenesis of FFA is multifactorial, with familial occurrence, some genetic markers, and associated clinical conditions; in the meantime, there is a global effort underway to find possible environmental triggers of disease development.1

Because FFA is an uncommon chronic disease, and most patients do not perceive the precise disease onset, exploratory studies based on disease incidence (eg, cohort studies) in a susceptible population are not reasonable. Furthermore, once the immunologic damage in the follicle has started, the investigation of environmental causality by removing an exposition (eg, prospective clinical trial) is less feasible. Therefore, a large case-control study is indeed the best option for assessing multiple expositions and constitutional risk factors toward formulating causality hypotheses.

Former case-control studies in Caucasoid populations suggested an association between FFA and the use of sunscreens and sunscreen-containing facial moisturizers.2 We assessed a multiracial population and found an association of FFA with formalin-based hair straightening, nondermatologic soap, and facial moisturizers, whereas FFA was not associated with sunscreens.3

The incidence of FFA is increasing worldwide. It is not exclusive to any kinds of hair; nor does it occur only in Caucasoids.4 In our supplementary Tables I and II (available via Mendeley at https://doi.org/10.17632/yczrjmjwb8.1), we disclosed results analyzed separately by fair or darker skin types.3 Sunscreen use was not associated with FFA, but formalin straightening and facial moisturizers remained associated in both subgroups, reinforcing the consistency of the results.3 Moreover, the association with sun exposure and the low prevalence among smokers and those living near agricultural fields were other intriguing factors suggested by our data.

Accessing distinct populations exposed to different factors is the best way to evaluate associations with initially disregarded elements. Regional questionnaire studies evaluating a series of patients would be intrinsically biased. The adequate evaluation of a control group pondering potential risk-related covariables, minimizes this bias. In our study, we chose patients from the same case centers, but with the diagnosis of nonscarring alopecia. The option of selecting patients with lichen planopilaris, an even rarer disease, as a control group is not feasible for a study that considers the effect of several variables.

Finally, case-control studies are suitable for raising hypotheses but not for proving a causal relationship. Correlation does not imply causality, but the latter depends first on a demonstration of the former.3 Nevertheless, we are not aware of any scientific correlational study that disregards statistics. Cooperative groups should work together to confirm the associations indicated in observational studies. The comparison of different populations and the effects of their skincare lifestyles on the incidence of FFA; molecular and immunologic studies evaluating the ingredients in sunscreens, moisturizers, and hair straighteners; investigation of the immunomodulation of the hair follicle by tobacco smoking or sun exposure; and the role of particulate air pollution are the next steps in understanding of environmental factors influencing FFA incidence.

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REFERENCES


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