Finasteride in Frontal Fibrosing Alopecia: Joining the Dots!

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Dear Editor,

5- α reductase inhibitors (5 α RI) such as finasteride and dutasteride have increasingly shown the best efficacy in the stabilization and improvement of frontal fibrosing alopecia (FFA) and also reversal of atrophy [1, 2]. A hormonal basis of the disease pathogenesis has been emphasized earlier on the basis of the prevalence of FFA in postmenopausal women with a high rate of early menopause or hysterectomy noted in some studies [1], which probably led to therapeutic trials of 5 α RI in FFA. However, the mode of action of these antiandrogens in an autoimmune disease remains elusive. Whether it treats the co-existing androgenetic alopecia (AGA) and enhances the residual hair density, or whether it has a direct role in arresting the lichenoid disease process is yet undefined. We hereby attempt to give a plausible explanation for the same.

FFA is a variant of lichen planopilaris (LPP), affecting predominantly the marginal scalp and eyebrows. The exact pathogenesis is unknown, but it is believed that there is preferential involvement of vellus-like/intermediate hairs, unlike terminal hairs, by the lymphocytic inflammatory infiltrate and fibrosis in FFA, as shown by Tosti et al. [3]. The susceptibility of vellus and intermediate hairs to FFA is a subject of debate, as these hairs are otherwise also more numerous in FFA-affected areas. In addition, whether it is linked to follicle size or shorter anagen duration is yet to be understood. Nevertheless, finasteride, by inhibiting the conversion of testosterone to dihydro-testosterone, causes reversal of miniaturization; i.e., it converts vellus/intermediate hairs to terminal hairs as well as prolongs the anagen duration. Furthermore,

these “terminalized” hairs then can escape the assault of the lichenoid pathology. Hence, finasteride with its anti-androgenic action, can contribute to the “follicular rescue” process in this scarring alopecia.

This hypothesis applies in certain other androgen-dependent areas as well. FFA is known to involve the occipital scalp margin also, where the role of finasteride would at first seem dubious, as the occipital region of the scalp represents an androgen-independent area. Ryu et al. [4] demonstrated that the ratio of the scalp skin dihydro-testosterone to testosterone does not decrease with finasteride in the occipital scalp. Interestingly, the lower occipital area; i.e., the occipital margin of the scalp, is actually involved in miniaturization as part of AGA, as was originally described in male-pattern hair loss by Hamilton [5] in 1951, which has somehow lost attention in recent times. Hence, finasteride, by reversal of miniaturization, acts by arresting the progression of FFA at the occipital scalp as well.

In recent years, the prevalence of FFA is being increasingly recognized in premenopausal women and men [6]. A study on serum sex hormone levels in 43 premenopausal women has reported no consistent alterations, suggesting that sex hormone levels are not directly implicated in the pathogenesis of FFA [7]. However, a potential hormonal involvement by a local mechanism; i.e., end-organ hypersensitivity to androgens, as is noted in AGA, cannot be excluded. Hence, the above hypothesis on the role of 5 α RI in FFA holds true for the treatment in premenopausal women as well, but these drugs must be administered with adequate contraceptive measures.

Fibrosing alopecia in pattern distribution (FAPD) is another recently described variant of LPP, wherein the frontal scalp is diffusely involved in scarring [8]. FAPD shares many features with FFA, as both represent scarring alopecia, but in a distribution of a typically female-pattern and male-pattern AGA, respectively [9]. Hence, the selective involvement of miniaturized hairs by lichenoid inflammatory infiltrate seems likely in both these entities. Zinkernagel and Trüeb [8] have reported improvement with finasteride in a patient of FAPD. Finasteride has also been tried successfully by Mardones et al. [10] in 4 women who were not stabilized using topical minoxidil and clobetasol alone. This can also be explained by a similar mechanism of action of finasteride, namely, to help rescue “predisposed” vellus/intermediate follicular units by reversing the miniaturization, as in FFA.

While the above points clearly support our hypothesis on the beneficial role of finasteride in FFA, on the other hand, there are some contradictory findings in the literature. Firstly, eyebrow improvement has been reported by Georgala et al. [11] in 6 out of 7 patients of FFA after 1 year of oral dutasteride. This cannot be explained by the above-mentioned hypothesis on finasteride, as this drug cannot transform a normal vellus-like/intermediate hair like that of an eyebrow, into a terminal follicle. Secondly, although vellus/intermediate hairs have been observed to be more commonly affected, terminal hairs are also affected at the same time. The mechanism of action of 5 α RI on terminal hairs is difficult to explain. Hence, further studies need to be directed to decipher the exact pathogenesis of the disease and therapeutic role of these drugs.

By far, the above plausible hypothesis on the role of finasteride in FFA and FAPD only highlights the underlying pathophysiology of these two diseases. Unlike LPP, only the target vellus/intermediate hair follicles in FFA might express certain biological markers that induce a lymphocytic reaction leading to follicular destruction and scarring [3, 12]. As also highlighted by Olsen [9] in 2005, further research needs to be done to unveil the potential role of androgens in the development of inflammatory reaction in the scalp. Till then, these drugs offer a good therapeutic option to halt the disease process in an indirect way.

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