Treating Androgenetic Alopecia: A Review of Medical Treatments

In this second part of a two-part series on androgenetic alopecia, physicians who treat hair loss discuss the medication treatments in their armamentarium and the factors that determine their treatment choices.

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Moderate to extensive hair loss occurs in an estimated 53% of men[1] and 25% of women[2] by age 49. Further, hair loss can greatly affect the self-image and subsequently quality of life.[3-5] For many patients, the cause is androgenetic alopecia (AGA), a genetically influenced disorder characterized by the gradual conversion of terminal hairs into indeterminate, and eventually, vellus hairs.

People who experience hair loss often turn to their family physician, dermatologist, or even a hair loss specialist to determine the cause and, more importantly, how to treat it. Treatment typically includes a topical preparation and/or prescription oral medication. The majority of people who seek treatment receive one or both of these options, but a small minority leave their doctor's office without a prescription or a plan. The most common reason for that, at least for men, is the realization that treatment requires a commitment that the patient is not willing to make.

"Some ask '*You mean I have to do this every day?*', and I reply '*Probably forever,*'" said Justin Bailey, MD, of the Family Medicine Residency of Idaho in Boise. When he informs his patients that treatment cessation will cause the loss of any benefits gained, patients may choose to go bald due to the long-term maintenance of treatment, he said.

"I would say approximately 5% of patients are given no treatment and that is because of their choice," said Omer Ibrahim, MD, a dermatologist with Chicago Cosmetic Surgery and Dermatology in Illinois. "The characteristics of these patients are almost always male because balding as a man is socially acceptable. Balding as a woman is much less acceptable."

When patients choose to pursue treatment—which, according to the 15 physicians interviewed, is a vast majority of patients who consult a doctor for hair loss—their treatment varies based on a number of factors. For example, the specialty of the practitioner may be critical, as dermatologists and hair loss specialists are likely to be more familiar with and comfortable prescribing medications than primary care physicians. Patient sex and administration preference can also play a role. Some patients prefer the ease of taking a pill to rubbing a topical solution through their hair twice a day, while others prefer the perceived safety of a topical vs an oral medication. Potential side effects of treatments, including teratogenicity and decreased libido, influence or even dictate treatment choices for women of childbearing potential and men.

In the second article of this two-part series on AGA treatment,[6] we discuss providers' choices of treatment for AGA and, importantly, how the patient's sex can influence those choices.

Topical Treatment is Top Choice

Dermatologists, family practitioners, and hair loss specialists, regardless of specialty, said they begin with topical minoxidil due to its low cost, availability, and safety.

"Topicals are safer than orals," said Wilma Bergfeld, MD, professor of dermatology and pathology at the Cleveland Clinic Educational Foundation. Marc Avram, MD, a hair transplant specialist and cosmetic dermatologist in New York City, NY, also noted that minoxidil is popular because it is available as an over-the-counter (OTC) product. "It's approved for men and women. It's cost effective," he said.

As the only FDA-approved topical for AGA, minoxidil is available OTC in 2% and 5% topical cream solutions and in a 5% foam formulation, but it is also available as an oral tablet with a prescription. Although the mechanism by which topical minoxidil works on hair loss is not well understood, research has suggested at least a few possibilities: inhibiting apoptosis of epidermal cells; prolonging the survival time of keratinocytes; and opposing calcium entry into the cells, leading to an increased in epidermal growth factors.[7]

Some physicians, including Scott A. Boden, MD, of Hair Restoration Center of Connecticut in Wethersfield, CT, noted using used topical minoxidil equally in men in women. "I recommend topical minoxidil for all of my male and female patients," he said. Others said the sex of the patient factors into their decision to prescribe a topical, with a group of physicians prescribing topicals more commonly (some dramatically so) for one sex than the other.

"If we're talking about men, I recommend [topicals] to almost all of them," said Ivan S. Cohen, MD, of the Center for Hair Transplantation in Fairfield, CT. "I'd say in women, I probably use a topical in 75% of them and the rest I treat with oral minoxidil."

For Daniel Hoffman, MD, a family medicine physician in Dunlap, IL, topicals are the first choice for women, not men, for compliance reasons. "For women, I'll usually give more topicals. The men I'll usually give orals," he said, explaining that he anecdotally finds women more willing to use topicals as directed. "Women continually comb their hair. They wash their hair. They take care of their hair," he said. "Men do not do that generally. So, it's easier to say to a woman, *'Put this on twice a day,'* and she'll follow your directions. You tell a man to do it—not happening. So, it is a lot easier to say, *'When you get up in the morning, take the pill. If you don't want to take in the morning, take it in the evening, but take it.'"*

Marc Glashofer, MD, a board-certified dermatologist of The Dermatology Group in northern New Jersey, has found the opposite to be true. "So, a lot of women do not like doing minoxidil," he explained. "They feel like it messes the hair up. It's tough to do styling. It causes irritation. It can cause dry hair." For that reason, he said, only about half of his female patients use it.

Oral Therapy Options

When topical treatment is not preferred or does not produce desired results, the doctors interviewed typically turn to oral medications. Oral treatment consists of three options: minoxidil, finasteride, or spironolactone. Of those, only finasteride is FDA-approved to treat male pattern hair loss (MPHL).[8] Oral minoxidil is an antihypertensive agent with mild antiandrogenic effects that has been shown to help with hair loss in both men and women.[9] Spironolactone is a potassium-sparing diuretic and moderate antiandrogen with the side effect of promoting hair growth.[2]

The choice of oral treatment, interviews revealed, may depend on the severity of hair loss, patient comorbidities, the comfort with oral therapy of the physician and patient, and the patients' sex. "It just depends on how bad their hair loss is, what their preferences are, and what their other comorbidities might be," said Nicole Rogers, MD, of Hair Restoration of the South in Metairie, LA. Use of the three oral options varied widely among the physicians interviewed.

Minoxidil. Use of oral minoxidil ranged from "a lot" by Carlos Puig, MD, of Physicians Hair Restoration Center in Houston, TX, to "never" among some of the doctors, citing side effects and unfamiliarity with the drug as the main reasons for not prescribing it.

"I have never prescribed oral minoxidil," said family physician Dr Bailey. "I've just used the topical. I know that's an option, but usually I've left that for my dermatologist colleague."

"I don't typically prescribe oral minoxidil because there can be systemic side effects, including drop in blood pressure and higher potential for fluid retention. I commonly consider prescribing higher concentration minoxidil lotion, and this can be combined with topical finasteride," said Dr Boden.

Other physicians, including Dr Cohen, say they use oral minoxidil frequently in certain patient groups. While Dr Cohen rarely prescribes it for men, he said he uses "a fair amount of oral minoxidil" in middle-aged and older women. "I use it infrequently in younger women," he says. "But in older women, probably 50% are on that drug, and the other 50% on oral finasteride."

Finasteride. Similarly, doctors varied in their use of finasteride but were more likely to prescribe it for men.

"Oral finasteride is a bedrock of medical therapy for male pattern hair loss for my patients," said Vladimir Ratushny, MD, PhD, a Harvard-trained dermatologist and hair transplant surgeon from Massachusetts Dermatology Associates and MassDerm Hair Transplant Institute in Beverly. "Finasteride has the highest efficacy of all the medical treatments for male pattern hair loss." Similarly, Dr Puig added that he uses and recommends finasteride to all men.

While finasteride is approved only for men, the majority of physicians interviewed prescribed it in at least a small percentage of their female patients. Most said they used it cautiously in women and reserved it only for those beyond child-bearing age.

"I'm cautious of prescribing oral finasteride to women, despite some data showing its efficacy in female pattern hair loss," said Dr Ratushny. "The reasons behind my reservation to prescribe it is it can be teratogenic to male fetuses if given to premenopausal women. Additionally, it may have an effect on altering hormonal levels. I always review the potential risks of oral finasteride with any patients to whom I consider prescribing it."

But even when prescribing it to men, doctors can encounter some obstacles, noted Dr Cohen. "A lot of men are freaked out about taking oral finasteride. I have to explain to them that it is a very low percentage who experience sexual side effects. I can get most of them to take it, but a good percentage of them do not want to take the pill because they read junk on the internet and they just won't take it."

Spironolactone. Spironolactone was the least frequently prescribed by most of the doctors interviewed. It is reserved for women, particularly those for whom other treatments have not helped.

"I have seen my female pattern hair loss patients experience beneficial results from spironolactone," said Dr Ratushny. "Maybe in 30% to 40% of patients, I do see some benefit of it. If anything, it may slow down their hair loss."

"You obviously don't use spironolactone in men," said Dr. Cohen. "I probably use it in 20% of younger women."

"I do use a lot of spironolactone in women and love it," said Dr Rogers. "Besides improving hair loss in women, it helps with acne and unwanted facial hair. Their menses often become lighter and shorter. Women with early thinning can stabilize their hair loss with 50 to 100 mg daily. Women with more advanced hair loss can regrow hair with a dose of 100 to 200 mg, but they require some laboratory monitoring of the kidney function and electrolytes. For women past menopause, I agree with my colleagues that finasteride is generally easier to prescribe with fewer side effects. I usually prescribe it at a 5-mg dose in women, because the one and only clinical trial done in women showed no efficacy with the 1-mg dose."

Some physicians, including Dr Puig, rarely use spironolactone in any type of patient. "I don't typically use spironolactone," he said. "The reason why I don't is that it has a large number of side effects and my practical experience is that I've seen probably more treatment failures with spironolactone than any other medication used for hair loss."

Combination Approaches

The majority of physicians said they use two or more treatments, with medication or non-medication options, in combination to achieve results through various modalities. "I try to get most of my patients on a combination treatment because it's a synergistic effect," explained Dr Glashofer.

"These therapies all have different mechanisms of action," said Dr Puig. "Our practical experience is that they're synergistic." Dr Ratushny noted using multiple treatments in 80% to 90% of his patients because of the complementary effects as well.

As with individual drugs, combinations may vary by the patient's sex. "I have a lot of male patients on combination therapy, minoxidil and finasteride—go-to medications for most men," said Dr Cohen.

"For example, for male patients, [I recommend] oral finasteride and topical minoxidil," said Dr Ratushny. "For female patients, I usually recommend topical minoxidil and possibly oral spironolactone or recommend low-level light therapy for them."

"So, for women, platelet-rich plasma, low-level light therapy, and minoxidil are all popular treatment options," said Dr Avram.

New Technology in Development

As the experts noted, sex has limited treatment choices for patients with AGA. Drugs that block androgens, which are effective for many women, can have feminizing effects on men, whereas estrogens, which are limited in women due to adverse side effects, are completely off limits to men. Emerging technology may offer a wider variety of options for AGA.

Currently in development is a therapy that uses soft agonists and antagonists of topical hormone receptors to locally target estrogen and androgen receptors on the skin and mucous membranes of both men and women without systemic side effects. This soft estrogen technology is currently used in a line of skin creams to restore moisture and elasticity to estrogen-deficient skin due to aging.[10] The company behind the technology, OrGenix Therapeutics, now has locally acting androgen receptor antagonists in preclinical testing for AGA.

Another product in the works is a once-daily topical that could be an alternative to topical minoxidil, which requires a twice-daily application that can be seen as a hassle to patients. Developer Exicure is focusing its efforts on technology that uses nanoscale constructs consisting of synthetic nucleic acid sequences. Further, they have partnered with Allergan to develop this treatment in addition to another for hair loss disorders.[11]

One potential therapeutic option in the treatment of AGA is the Wnt pathway. Developer Samumed has identified another molecule, SM04554, that disinhibits the Wnt pathway to transition the telogen phase of hair follicles to the anagen phase. The company has begun clinical trials that test the efficacy and safety of the topical therapeutic at 0.15% & 0.25% concentrations.[12]

In addition to the current anti-androgens, another product in development is a topical clascoterone solution 7.5% by Cassiopea. This new therapy is thought to prevent dihydrotestosterone from binding with androgen receptors within the sebaceous gland and hair follicles. Phase 2 clinical trial of the product for men with AGA has been completed,[13] and a phase 2 trial for women with AGA is now underway.[14]

Patient Satisfaction

While the experts would welcome improvements in the therapeutic options for hair loss, they expressed general satisfaction with the current treatments and combinations, with most patients who are willing to adhere to treatment experiencing some slowing of hair loss or growth of new hair.

"I would say about 90% to 95% of my patients will stop losing hair," said Dr Boden. "About 30% to 40% will actually have some regrowth of miniaturized hair."

"I'm pretty satisfied. [For] most people, we can slow the progression at least," echoed Dr Cohen. "Most patients do well. The problem is a lot of them just give up on the treatment and they say *'I don't care anymore.'* But if they stay on it, most people do well." ■

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