Androgenetic Alopecia: What Works?

Jeff Donovan, MD, PhD

When it comes to selecting medical treatments for androgenetic alopecia (AGA), patients and practitioners alike want to know, "What works?" The ideal AGA treatment is one that meets 4 criteria: highly effective, safe, affordable, and easy to use. To date, there is no known treatment for AGA that meets all these criteria. Some therapies are more effective than others, but there are no treatments at present that are able to completely and permanently reverse the condition. Some treatments are safer, some are less expensive, and some are easier to use than others. In the end, the treatment that the patient chooses is influenced not only by its known effectiveness but also by the value that the patient places on the other 3 categories—safety, affordability, and ease of use. Therefore, shared decision-making between patient and practitioner is central to the selection of specific AGA treatments.

Effectiveness: Some Treatments Work Better Than Others

Of the nearly 2 dozen medical treatments for AGA, some have been found to be more effective than others. Whether a given treatment should be considered a bona fide AGA therapy—and then whether to position it as a first-line, second-line, or third-line agent—depends on the answers to 3 fundamental questions:

1. Does the treatment truly help patients with AGA?
2. How effective is this treatment?
3. How safe is it?

Does the Treatment Truly Help Patients?—Surprisingly, it is not always straightforward to confirm that a given treatment helps patients with AGA. Does oral finasteride help female AGA? Yes and no: Finasteride 1 mg is ineffective in the treatment of female AGA, but higher doses such as 2.5 or 5 mg likely have benefit.[1,2] Does topical minoxidil help AGA? Yes and no: Minoxidil 5% is ineffective in the treatment of a male with Hamilton-Norwood stage VII AGA but often is helpful in earlier stages of the condition.

One of the best ways to determine if a treatment really helps AGA is to evaluate how it performs in the setting of a well-conducted, randomized, double-blind, placebo-controlled trial. These types of clinical trials have been performed for many known AGA treatments and give us some of the best evidence that a treatment truly works. The AGA treatments with the highest-quality evidence (level 1) are topical minoxidil, oral finasteride, and oral dutasteride for male AGA and topical minoxidil for female AGA.

How Effective Is This Treatment?—Patients are particularly interested to know whether a given treatment has the potential to notably restore hair density. It is one thing to know that use of the treatment might slightly improve hair density and another to know that it could potentially lead to dramatic improvement. In addition, patients want to know whether a specific treatment they are considering is more (or less) likely to improve their hair density compared to another treatment.

Advanced statistical methods such as the network meta-analysis are increasingly being used to understand how individual treatments from different studies compare. Two recent studies have provided us with powerful data on the relative efficacy of minoxidil and 5α-reductase inhibitors in the treatment of both male and female AGA.[2,3] A 2022 network meta-analysis of male AGA ranked treatment efficacy from most to least effective: oral dutasteride 0.5 mg, oral finasteride 5 mg, oral minoxidil 5 mg, oral finasteride 1 mg, and topical minoxidil 5%.[3] Similarly, a 2023 network meta-analysis of female AGA ranked treatment efficacy from most to least effective: oral 5 mg finasteride, minoxidil solution 5% twice daily, oral minoxidil 1 mg, and minoxidil foam 5% once daily.[2] We are not yet able to rank all known treatments for AGA.

Things We Tend to Ignore: Quality of Data, Long-term Results, Nonresponders, and Study Populations—There are a few caveats for anyone treating AGA. First, the quality of published AGA studies is highly variable and many are of low quality. The highest-quality evidence (level 1) for male AGA comes from studies of minoxidil solution/foam 5% twice daily, oral finasteride 1 mg, and oral dutasteride 0.5 mg. For female AGA, the highest-quality evidence is for topical minoxidil—either 5% foam once daily or

From the Donovan Hair Clinic, Whistler, British Columbia, Canada, and the Department of Dermatology, University of British Columbia.
Dr. Donovan has received honoraria from Pfizer, UpToDate, and Vichy.
Correspondence: Jeff Donovan, MD, PhD, Donovan Hair Clinic, 4370 Lorimer Rd, Ste 334B, Whistler, BC V8E 1A6, Canada (office@donovanmedical.com).
doi:10.12788/cutis.0924

2% solution twice daily. Lower-quality studies limit conclusions and the ability to properly compare treatments.

Second, long-term data are nonexistent for most of our AGA treatments. The exceptions include finasteride, dutasteride, and topical minoxidil, which have reasonably adequate long-term studies.[4-6] However, most other treatments have been evaluated only through short-term studies. It is tempting to assume that results from a 24-week study can be used to infer how a patient might respond when using the same treatment over the course of many decades; however, making these assumptions would be unwise.

Third, most AGA treatments help improve hair density in only a proportion of patients who decide to use the given treatment. There usually is one subgroup of patients for whom the treatment does not seem to help much at all and one subgroup for whom the treatment halts further hair loss but does not regrow hair. For example, in the case of finasteride treatment of male AGA, approximately 10% of patients do not seem to respond to treatment at all, and another 50% seem to be able to halt further loss but never achieve hair regrowth.[7] In an analysis of 12 studies with 3927 male patients, Mella et al[8] showed that 5.6 patients needed to be treated short term and 3.4 patients needed to be treated long term for 1 patient to perceive an improvement in the hair. It is clear that many males who use finasteride will not see evidence of hair regrowth. This same general concept applies for all available treatments and is important to remember if a patient with AGA decides to start 2 new treatments simultaneously. Consider the 34-year-old man who starts oral minoxidil and platelet-rich plasma (PRP) for AGA. At his follow-up appointment 9 months later, the patient reports improved hair density and wants to know what contributed to the improvement: the oral minoxidil, the PRP, or both? Many practitioners would believe that both treatments likely provided some degree of benefit—but in reality, that represents a flaw in logic. If 2 hair loss treatments are started at exactly the same time, it is impossible to know the relative benefit of each treatment and whether one might not be helping at all. Combination therapies are still common in my practice and highly encouraged, but my personal preference is to stagger start dates whenever possible so I can determine each treatment's contribution to the patient's final outcome.

Finally, when evaluating what works for AGA, we need to define the specific patient subpopulation, as the available data are less robust for some patient groups than others. We have limited data in children and adolescents with AGA, as well as limited comparative data across different racial backgrounds, body mass indices, and underlying health issues. For example, data on the most effective strategies to treat female AGA in the setting of polycystic ovary syndrome, premature menopause, and other endocrine disorders are lacking.

Which Treatments Also Have Good Safety?—The treatment that a patient ultimately selects also depends on its actual or perceived safety. Patients have vastly different levels of risk tolerance. Some patients would much rather start a less effective treatment if they believe that the chances of experiencing treatment-related adverse effects would be lower. In general, topical and injectable treatments tend to have fewer adverse effects than oral therapies. Long-term safety data generally are lacking for many hair-loss therapies. A limited number of studies of topical minoxidil include data up to 5 years,[4] and some studies of oral finasteride and oral dutasteride include patients who used these medications for up to 10 years.[5,6]

So Then, What Works?

The Table shows treatments for AGA and how I prioritize starting them in my own clinic. First-line treatment options often include those with level 1 evidence but also may include those with less-robust evidence plus a good history (over many years) of safety, affordability, ease of use, and effectiveness (eg, spironolactone and finasteride for female-pattern hair loss).

- Male AGA: I consider topical minoxidil, oral finasteride, and oral dutasteride as first-line agents, and low-level laser, PRP, oral minoxidil, and topical finasteride as second-line agents. Only topical minoxidil and oral finasteride are approved by the US Food and Drug Administration (FDA) for AGA in males; laser devices are FDA cleared.
- Premenopausal females with AGA: I use topical minoxidil and spironolactone as first-line agents. Low-level laser, PRP, oral minoxidil, and oral contraceptives are helpful second-line agents. Only topical minoxidil is FDA approved in women. I consider all treatments, with the exception of low-level laser, to be contraindicated in pregnancy.
- Postmenopausal females with AGA: I consider topical minoxidil, spironolactone, and oral finasteride as first-line agents. Low-level laser, PRP, oral minoxidil, and oral dutasteride are helpful second-line agents.

When choosing an initial treatment plan, I generally will start with one or more first-line options. I will then add or replace with remaining first-line options or a second-line option after 6 to 12 months depending on how well the patient responds to the first-line options. Patients who do not wish to use first-line options or have contraindications begin with second-line options. Third-line options are best reserved for patients who do not respond to or do not wish to use first- and second-line options.

Experts differ in opinion as to what constitutes a first-line treatment option and what constitutes a second- or third-line option. For example, some increasingly consider oral minoxidil to be a first-line option for AGA.[9] In my opinion, the lack of high-quality comparative, randomized, controlled trials and long-term safety data keep oral minoxidil reserved as a respectable second-line option. Similarly, some experts reserve oral dutasteride as a second-line option for AGA.[10] In my opinion, the data now are of the highest-quality evidence (level 1)[9] to support placing oral dutasteride in the tier of first-line treatments.

Treatment of Androgenetic Alopecia

Treatment tier	Treatment options
Males	
First line	Topical minoxidil, oral finasteride, oral dutasteride
Second line	Photobiomodulation, platelet-rich plasma, oral minoxidil, topical finasteride
Third line	Antiandrogen mesotherapy, topical dutasteride, topical minoxidil 6%–15%, microneedling, botulinum toxin therapies, nutraceuticals
Unclear or of interest for further study	Exosomes, topical melatonin, topical latanoprost, pumpkin seed oil, topical caffeine, topical cetirizine
Premenopausal females	
First line	Topical minoxidil, spironolactone
Second line	Photobiomodulation, platelet-rich plasma, oral minoxidil, oral contraceptives
Third line	Finasteride, antiandrogen mesotherapy, bicalutamide, topical finasteride, topical minoxidil 6%–15%, microneedling, nutraceuticals
Unclear or of interest for further study	Exosomes, topical melatonin, topical latanoprost, topical caffeine, topical cetirizine, topical spironolactone
Postmenopausal females	
First line	Topical minoxidil, spironolactone, oral finasteride
Second line	Photobiomodulation, platelet-rich plasma, oral minoxidil, oral dutasteride
Third line	Antiandrogen mesotherapy, bicalutamide, topical finasteride, topical minoxidil 6%–15%, microneedling, nutraceuticals
Unclear or of interest for further study	Exosomes, topical melatonin, topical latanoprost, topical caffeine, topical cetirizine, topical spironolactone

Shared decision-making using an evidence-based approach is ultimately what connects patients with treatment plans that offer a good chance of helping to improve hair loss.

REFERENCES

1. Price VH, Roberts JL, Hordinsky M, et al. Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. *J Am Acad Dermatol*. 2000;43(5 pt 1):768-776. doi:10.1067/mjd.2000.107953
2. Gupta AK, Bamimore MA, Foley KA. Efficacy of non-surgical treatments for androgenetic alopecia in men and women: a systematic review with network meta-analyses, and an assessment of evidence quality. *J Dermatolog Treat*. 2022;33:62-72. doi:10.1080/09546634.2020.1749547
3. Gupta AK, Wang T, Bamimore MA, et al. The relative effect of monotherapy with 5-alpha reductase inhibitors and minoxidil for female pattern hair loss: a network meta-analysis study [published online June 29, 2023]. *J Cosmet Dermatol*. doi:10.1111/jocd.15910
4. Olsen EA, Weiner MS, Amara IA, et al. Five-year follow-up of men with androgenetic alopecia treated with topical minoxidil. *J Am Acad Dermatol*. 1990;22:64.
5. Choi G-S, Sim W-Y, Kang H, et al. Long-term effectiveness and safety of dutasteride versus finasteride in patients with male androgenic alopecia in South Korea: a multicentre chart review study. *Ann Dermatol*. 2022;34:349-359. doi:10.5021/ad.22.027
6. Rossi A, Cantisani C, Scarnò M, et al. Finasteride, 1 mg daily administration on male androgenetic alopecia in different age groups: 10-year follow-up. *Dermatol Ther*. 2011;24:455-461.
7. Kaufman KD, Olsen EA, Whiting D, et al. Finasteride in the treatment of men with androgenetic alopecia. Finasteride Male Pattern Hair Loss Study Group. *J Am Acad Dermatol*. 1998;39(4 pt 1):578-89. doi:10.1016/s0190-9622(98)70007-6
8. Mella JM, Perret MC, Manzotti M, et al. Efficacy and safety of finasteride therapy for androgenetic alopecia: a systematic review. *Arch Dermatol*. 2010;146:1141-1150. doi:10.1001/archdermatol.2010.256
9. Vañó-Galván S, Fernandez-Crehuet P, Garnacho G, et al; Spanish Trichology Research Group. Recommendations on the clinical management of androgenetic alopecia: a consensus statement from the Spanish Trichology Group of the Spanish Academy of Dermatology and Venererology (AEDV). *Actas Dermosifiliogr*. 2023 Oct 25:S0001-7310(23)00844-X. doi:10.1016/j.ad.2023.10.013. Online ahead of print.
10. Kanti V, Messenger A, Dobos G, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men - short version. *J Eur Acad Dermatol Venereol*. 2018;32:11-22. doi: 10.1111/jdv.14624