Clinical Review:

Topical Management of Alopecia

Alopecia affects a significant number of Americans. One study of men between the ages of 18 to 49, found that 42% of the men had moderate to extensive hair loss.1 Hair loss is less prevalent in women and has a reported incidence of between 29 to 38% in women over 70 years of age.2 There are a variety of different pathologies that can contribute to hair loss including noncicatricial alopecias such as androgenic alopecia, alopecia areata, and telogen effluvium as well as cicatricial alopecias such as lichen planopilaris. Androgenetic alopecia is the most prevalent form of hair loss in both men and women.3 In this newsletter, we will focus on noncicatricial alopecias and review topical treatments and their evidence for efficacy for various types of hair loss.

The most common variety of hair loss, androgenetic alopecia, has been well studied. It can be precipitated by acute stressors, weight loss, drugs (including contraceptives that contain androgenic progestins), and of course, has a strong genetic component.4 It is called androgenetic alopecia in reference to its mechanism of action, which is dihydrotestosterone (DHT) causing hair follicle miniaturization. This type of alopecia grows more common with advancing age. Conversely, alopecia areata often onsets before the age of 30, and hair loss is caused by autoimmune destruction of hair follicles. Alopecia areata often looks distinct from androgenetic alopecia, rather than causing thinning and hairline recession, alopecia areata tends to cause round areas of total hair loss and oddly shaped hairs called exclamation point hairs. Other types of noncicatricial alopecia include telogen and anagen effluvium. Telogen effluvium is diffuse hair loss and can usually be attributed to a stressor event, generally occurring several months before the hair loss is seen. This hair loss is the result of 20-50% of scalp hair transitioning to the telogen phase prematurely. Anagen effluvium is also characterized by diffuse hair loss but is also associated with hair breakage during the anagen phase, and generally occurs within 1 to 4 weeks of a precipitating event such as radiation therapy or chemotherapy.5 In this article, we will be focusing on topical treatments for the two most common types of alopecia; alopecia areata, and androgenetic alopecia.

Topical minoxidil has been well studied in both men and women at both 2% and 5%. Studies have demonstrated the superior efficacy of 5% minoxidil over 2% minoxidil twice daily. One study reported 45% more hair growth at week 48 of the study in the 5% minoxidil group. However, this increase in efficacy was tempered with increased adverse effects including pruritis and local irritation.4,6 Finasteride is another commonly used agent for androgenic alopecia. Though the use of oral finasteride for alopecia is well documented, limited information exists on topical finasteride. Finasteride at concentrations of 0.005% have been tested in men and women and statistically, a significant benefit was observed after 6 months of use.7 Another 6-month long study in men tested a 1% finasteride gel formulation vs finasteride oral tablets and found efficacy with the topical gel.8 A more recent study of androgenic alopecia in men tested 0.25% finasteride in combination with 3% minoxidil vs 3% minoxidil alone over the course of 24 weeks and concluded that the combination therapy was significantly superior to minoxidil alone.9,10 Tretinoin is another topical option sometimes used. One study of once-daily tretinoin 0.01% with minoxidil 5% vs twice-daily minoxidil 5% found that the once-daily combination therapy was as effective as the twice-daily minoxidil treatment.12 Ketoconazole may also play a role in the treatment of androgenic alopecia. Limited studies in humans of ketoconazole 2% lotion or shampoo have shown benefit for some patients, and other studies in mice have noted hair regrowth as well, though the improvement was not as significant as minoxidil compared to the placebo group.13,14,15,16

Spironolactone is another agent sometimes used topically for hair loss. Very little information exists

concerning the use of this ingredient. One study of 60 female patients found a spironolactone 1% topical to be effective at promoting hair growth, however, the study has not been repeated and the benefit has not been studied in men.17,18 Estradiol is another topical option with some limited data in female alopecia. One 6-month long study evaluating estradiol 0.025% topical lotion in patients with androgenetic alopecia found a decrease in hair loss, however, regrowth of new hairs was not demonstrated. A possible mechanism is an estrogeninduced increase in glycoprotein sex hormone-binding globulin leading to decreased free testosterone.19 Yet another mechanism that may play a role in hair loss is prostaglandin-mediated anagen induction. Latanoprost and bimatoprost are both prostaglandin analogues generally used for glaucoma, however, recent evidence has emerged suggesting that in addition to their effect on increased eyelash growth, they may also be able to promote increased hair growth. One study in patients suffering from androgenetic alopecia found increased hair density observed with latanoprost 0.1% solution at 24 weeks as compared to placebo.20 Lastly, though the mechanism of action is at this point unclear, topical melatonin has also been associated with an increase in anagen hair in women with both diffuse and androgenetic alopecia. Melatonin 0.1% solution was applied to the scalps of these women for 6 months resulting in increased hair growth as compared to the placebo group.21,22
Some common treatments for alopecia areata include agents used to cause contact dermatitis including squaric acid and diphencyclopropenone. One study looking at diphencyclopropenone sensitized patients with a 2% solution before decreasing to a much lower concentration, usually 0.001%, after two weeks and then gradually increased dosing weekly thereafter up to the tolerated dose. The study had a response rate of 77% in patients with alopecia areata, and even saw some benefit in patients suffering from alopecia totalis and universalis.31,35 Squaric acid has a similar treatment protocol. One study started at 2% for an initial sensitization treatment before decreasing to 0.001% after one to two weeks. Then, much like with diphencyclopropenone, the dose was increased on a weekly basis until the patient had a reaction generally landing in the 0.01-1% range. The study found “excellent response” in 60% of treated sites.37 Other common active ingredients for the management of alopecia areata include steroids. One study of 28 patients with alopecia areata who applied 2.5g of 0.05% clobetasol propionate ointment for 6 months to one side of scalp resulted in some regrowth for 28.5% of patients.26 Studies of other potent steroids including betamethasone and fluocinolone acetonide also found benefit in patients suffering from alopecia areata.
There exists a myriad of treatments for alopecia, many more than have been documented above, if you would like to read more about other active ingredients and their possible roles in the management of various types of alopecia, head to the Fagron Academy website to see a table of actives, mechanism of action, concentrations, and study results.

Sources:

1. Rhodes T, Girman C, Savin R. Prevalence of male pattern hair loss in 18-49 year old men. Dermatol Surg. 1998; 24(12):1330-2.
2. Levy L, Emer J. Female pattern alopecia: current perspectives. Int J Womens Health. 2013; 5: 541-556.
3. Gordon K, Totsi A. Alopecia: evaluation and treatment. Clin Cosmet Investig Dermatol. 2011; 4: 101-106.
4. Olsen E, Dunlap F, Funicella T. A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men. J Am Acad Dermatol. 2002; 47)3):377-85.

5. Qi J, Garza L. An overview of alopecias. Cold Spring Harb Perspect Med. 2014; 4(3):a013615. 10.1101/cshperspect.a013615.
6. Hoedemaker C, van Egmond S, Sinclair R. Treatment of female pattern hair loss with a combination of spironolactone and minoxidil. Australas J Dermatol. 2007; 48(1):43-45.
7. Mazzarella F, Loconsole F, Cammisa A, Mastrolonardo M, Vena GA. Topical finasteride in the treatment of androgenic alopecia. Preliminary evaluations after a 16-month therapy course. J Dermatol Treat. 1997; 8: 189-92.
8. Hajheydari Z, Akbari J, Saeedi M, Shokoohi L. Comparing the therapeutic effects of finasteride gel and tablet in treatment of the androgenic alopecia. Indian J Dermatol Venereol Leprol. 2009; 1(75): 47-51.
9. Suchonwanit P, Srisuwanwattana P, Chalermroji N, Khunkhet S. A randomized, double-blind controlled study of the efficacy and safety of topical solution of 0.25% finasteride admixed with 3% minoxidil vs 3% minoxidil solution in the treatment of male androgenetic alopecia. J Eur Acad Dermatol Venereol. 2018;32(12):2257-2263. Doi: 10.1111/jdv/15171.
10. Won Lee S, Juhasz M, Mobasher P, Ekelem C, Mesinkovska N. A systemic review of topical finasteride in the treatment of androgenetic alopecia in men and women. Journal of Drugs in Dermatology. 2018; 4(17): 457-463.
11. Narasimhalu C. A cross-sectional randomized comparative study of topical minoxidil solution with and without finasteride in male pattern androgenetic alopecia in South Indian patients. International Journal of Research in Dermatology. 2018; 4(1):46-49.
12. Shin H, Won C, Lee S, Kwon O, Kim K, Eun H. Efficacy of 5% minoxidil versus combined 5% minoxidil and 0.01% tretinoin for male pattern hair loss. American Journal of Clinical Dermatology. 2007; 8(5): 285-290.
13. Inui S, Itami S. Reversal of androgenic alopecia by topical ketoconazole: relevance of anti-androgenic activity. Journal of Dermatological Science. 2007; 45(1): 66-68.
14. Pierard-Franchimont C, De Doncker P, Cauwenbergh G, Pierard G. Ketoconazole shampoo: effect of long-term use in androgenic alopecia. Dermatology. 19998; 196(4):474-7.
15. Jian J, Tsuboi R, Kojima Y, Ogawa H. Topical application of ketoconazole stimulates hair growth in C3H/HeN Mice. The Journal of Dermatology. 2005; 32(4):243-7.
16. Aldhalimi M, Hadi N, Ghafil F. Promotive effect of topical ketoconazole, minoxidil, and minoxidil with tretinoin on hair growth in male mice. ISRN Pharmacology. Vol 2014, Article ID 575423, 5 pages, 2014. https://doi.org/10.1155/2014/575423.
17. Dill-Muller D, Zaun H. Topical treatment of androgenetic alopecia with spironolactone. J Eur Acad Dermatol Venereol. 1997 Sep;9(Suppl 1):31.
18. Shamsaldeen O, Mubki T, Shapiro J. Topical Agents for Hair Growth Promotion: What is Out There. Skin Therapy Letter. 2013; 18(4): https://www.skintherapyletter.com/alopecia/growth-promotion/
19. Orfanos CE, Vogels L. [Local therapy of androgenetic alopecia with 17-alphaestradiol. A controlled, randomized, doubleblind study (author's transl)]. Dermatologica. 1980; 161(2):124-32
20. Blume-Peytavi U, Lonnfors S, Hillmann K, Garcia Bartels N. A randomized double-blind placebo-controlled pilot study to assess the efficacy of a 24-week topical treatment by latanoprost 0.1% on hair growth and pigmentation in healthy volunteers with androgenetic alopecia. J Am Acad Dermatol. 2012; 66(5): 794-800.
21. Fischer T, Burmeister, Schmidt, Elsner. Melatonin increases anagen hair rate in women with androgenetic alopecia or diffuse alopecia: results of a pilot randomized controlled trial. British Journal of Dermatology 2004; 150: 341-345
22. Fischer T, Trueb R, Hanggi G, Innocenti M, Elsner P. Topical melatonin for treatment of androgenetic alopecia. Int J Trichology. 2012; 4(4):236-245
23. Dhurat R, Chitallia J, May T et al. An open-label randomized multicenter study assessing the noninferiority of a caffeine based topical liquid 0.2% versus minoxidil 5% solution in male androgenetic alopecia. Skin Pharmacol Physiol. 2018; 30(6): 298- 305
24. Q Dinh, R Sinclair. Female pattern hair loss: current treatment concepts. Clin Interv Aging. 2007; 2(2):189-199

25. Lenane P, Macarthur C, Parkin P. Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata in children. JAMA Dermatol. 2014; 150(1):47-50. Doi:10.1001/jamadermatol.2013.5764
26. Tosti A, Piraccini B, Pazzaglia M, Vincenzi C. Clobetasol propionate 0.05% under occlusion in the treatment of alopecia totalis/universalis. J Am Acad Dermatol. 2003; 49(1):96-98
27. Micali G, Cicero R, Nasca M, Sapuppo A. Treatment of alopecia areata with squaric acid dibutylester. Int J Dermatol. 1996; 35(1):52-6
28. Chua S, Goh C, Ang C. Topical squaric acid dibutylester therapy for alopecia areata: a double-sides patient-controlled study. Ann Acad Med Singapore. 1996; 25(6):842-7
29. Zerbinati N, Esposito C, D'Este E, Calligaro A, Valsecchi R. Topical immunotherapy of alopecia areata: a large retrospective study. Dermatol Ther (Heidelb). 2018; 8(1): 101-110
30. Tiwary A, Mishra D, Chaudhary S. Comparative study of efficacy and safety of topical squaric acid dibutylester and diphenylcyclopropenone for the treatment of alopecia areata. North American Journal of Medical Sciences. 2016; 6(8): 237-242
31. Alsantali A. Alopecia areata: a new treatment plan. Clin Cosmet Investig Dermatol. 2011; 4:107-115
32. Mancuso G, Balducci A, Casadio C, et al. Efficacy of betamethasone valerate foam formulation in comparison with betamethasone dipropionate lotion in the treatment of mild-to-moderate alopecia areata: a multicenter, prospective, randomized, controlled, investigator-blinded trial. Int J Dermatol. 2003;42(7):572–575
33. Fiedler-Weiss V, Buys C. Evaluation of anthralin in the treatment of alopecia areata. Arch Dermatol. 1987; 123(11):1491-3
34. Fiedler V, Wendrow A, Szpunar G, Metzler C, DeVillez R. Treatment-resistant alopecia areata. Response to combination therapy within minoxidil plus anthralin. Arch Dermatol. 1990; 126(6):756-9
35. Wiseman M, Shapiro J, MacDonald N, Lui H. Predictive model for immunotherapy of alopecia areata with diphencyprone. Arch Dermatol. 2001; 137(8):1063-8
36. Das S, Ghorami RC, Chatterjee T, Banerjee G. Comparative assessment of topical steroids, topical tretinoin (0.05%) and dithranol paste in alopecia areata. Indian J Dermatol. 2010; 55(2):148-9
37. Inui S, Nakajima T, Toda N, Itami S. Fexofenadine hydrochloride enhances the efficacy of contact immunotherapy for extensive alopecia areata: retrospective analysis of 121 cases. J Dermatol. 2009; 36(6):323-7
38. Talpur R, Vu J, Bassett R, Stevens V, Duvic M. Phase I/II randomized bilateral half-head comparison of topical bexarotene 1% gel for alopecia areata. J Am Acad Dermatol. 2009; 61(4): 592.e1-9
39. Craiglow B. Topical tofacitinib solution for the treatment of alopecia areata affecting eyelashes. JAAD Case Rep. 2018; 4(10):988=989
40. Liu L, Craiglow B, King B. Tofacitinib 2% ointment, a topical Janus kinase inhibitor, for the treatment of alopecia areata: a pilot study of 10 patients. J Am Acad Dermatol. 2018; Research Letters:403-404
41. Kwon O, Han J, Yoo H et al. Human hair growth enhancement in vitro by green tea epigallocatechin-3-gallata (EGCG). Phytomedicine. 2007; 14: 551-555
42. Trueb R. Serum biotin levels in women complaining of hair loss. Int J Trichology. 2016; 8(2): 73-77.
43. Hosking A, Juhasz M, Atanaskova M. Complementary and alternative treatments for alopecia: a comprehensive review. Skin Appendage Disord 2019; 5: 72-89
44. Patel D, Swink S, Castela-Soccio L. A review of the use of biotin for hair loss. Skin Appendage Disord. 2017; 3(3): 166-169.
45. Jo SJ, Shin H, Park YW et al. Topical valproic acid increase the hair count in male patients with androgenetic alopecia: a randomized, comparative, clinical feasibility study using phototrichogram analysis. J Dermatol. 2014; 41(4): 285-91.
46. Rossi A, Campo D, Fortuna MC. A preliminary study on topical cetirizine in the therapeutic management of androgenetic alopecia. J Dermatolog Treat. 2018; 29(2): 149-151.
47. Harries M, Sun J, Paus R, King L. Management of alopecia areata. BMJ. 2010; 341: c3671.

48. Arican O, Sasmaz S. Comparison of azelaic acid and anthralin for the therapy of patchy alopecia areata: a pilot study. Am J Clin Dermatol. 2005; 6 (6): 403-6.
49. Pazoki-Toroudi H: The efficacy and safety of minoxidil 5% combination with azelaic acid 1/5% and caffeine 1% solution on male pattern hair loss (abstract). J Invest Dermatol 2013; 133:S84.
50. Gupta A. Azelaic acid: an update. JAAD. 2005; 52(3):P14.
51. Rafi A, Katz R. Pilot study of 15 patients receiving a new treatment regimen for androgenic alopecia: the effects of atopy on AGA. International Scholarly Research Notices. 2011. https://doi.org/10.5402/2011/241953.
52. Olsen E, Hordinsky M, Whiting D et al. The importance of dual 5alpha-reductase inhibition in the treatment of male pattern hair lss: results of a randomized placebo-controlled study of dutasteride versus finasteride. J Am Acad Dermatol. 2006; 55(6): 1014-23.
53. Boersma IH, Oranje AP, Grimalt R, Iorizzo M, Piraccini BM, Verdonschot EH. The effectiveness of finasteride and dutasteride used for 3 years in women with androgenetic alopecia. Indian J Dermatol Venereol Leprol. 2014;80(6):521–525. doi:10.4103/0378-6323.144162