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Review of the Efficacy of Topical 5-Alpha Reductase Inhibitors for the Treatment of Androgenetic Alopecia

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INTRODUCTION

Androgenetic alopecia (AGA) is a non-scarring alopecia triggered by an inherited follicular sensitivity to dihydrotestosterone (DHT) and other environmental factors.[1] Current FDA-approved treatments include topical minoxidil (in men and women) and oral finasteride (in men), often with varied efficacy. 5-Alpha-reductase inhibitors (5-ARIs), such as finasteride, inhibit dihydrotestosterone (DHT), but systemic absorption can lead to side effects such as sexual dysfunction and diminished libido. Recent trials have investigated topical 5-ARIs as a promising treatment for AGA, in hopes of obtaining the therapeutic benefit of these medications while limiting systemic exposure. This review investigates the efficacy of topical 5-ARIs in the treatment of AGA.

Articles regarding androgenic alopecia and topical 5-ARIs (including dutasteride, finasteride, and alfatradiol) were retrieved from PubMed, Embase, and Scopus Library databases. Two independent reviewers screened 340 articles, and 19 articles met the criteria for inclusion, available via Mendeley at https://data.mendeley.com/datasets/fdjwx97hwt/1 (Supplementary Figure 1). Quality of Evidence was assessed

TABLE 1.

Studies of Treatment With Topical 5-a-reductase Inhibitors Alone for AGA		
Study Design, total participants (N), participants receiving 5-ARIs (n), gender (M/F)	**Treatment Regimen; Duration (weeks)**	**Treatment Outcome *and effects on plasma DHT concentration (if reported)***
Randomized single-blind trial, N= 52, n = 28, M&F	0.005% FNS or placebo; 64 weeks	Decreased hair loss and higher treatment effectiveness after 2 months with FNS. *No change in plasma testosterone, free testosterone, or DHT levels.*
Open-label study, N= 103, n= 52, F	2% MNX or 0.025% alfatradiol for 6 months, then switched to MNX; 52 weeks	Hair thickness and density increased with MNX. *No change with Alfatradiol; improvement after switch to minoxidil.*
Randomized double-blind trial, N= 458, n= 189, M	0.25% FNS, oral placebo, or oral FNS; 24 weeks	Hair count increased in target area with 0.25% FNS vs. placebo; similar to FNS. *Lower reduction in serum DHT with topical vs. oral finasteride.*
Retrospective cohort, N= 120, n = 40, F	0.25% FNS, 2.5mg oral FNS, or 5% MNX; 52 weeks	0.25% FNS least effective for hair density and diameter. *No significant difference between groups.*
Randomized double-blind trial, N= 34, n= 34, M	TH07 (test product), 0.1% FNS, 0.03% latanoprost, or 5% MNX; 24 weeks	TH07 more effective than 0.1% FNS. *No reported difference between topical FNS, MNX, or latanoprost.*
Randomized double-blind trial, N=45, n =45 , M	1% FNS + placebo tablets, oral FNS 1 mg + placebo gel; 24 weeks	Terminal hair counts increased in both groups. *No significant difference between topical and oral FNS.*
Randomized single-blind trial, N=24, n = 12, M	0.25% FNS or oral FNS 1mg daily; one week	Similar plasma DHT inhibition with topical and oral FNS after 1 week. *Lower systemic exposure with topical finasteride.*

Abbreviations: DTS: dutasteride, FNS: finasteride, MN: microneedling, MNX: minoxidil

TABLE 2.

Studies of Treatment With Topical 5-a-reductase Inhibitors in Combination With Other Medications and/or Delivery Methods for AGA		
Study Design, total participants (N), participants receiving 5-ARIs (n), gender (M/F)	**Treatment Regimen; Duration (weeks)**	**Outcome and effects on plasma DHT concentration (if reported)**
Randomized single-blind trial, N=42, n =12 (FNS only) & 19 (FNS + MNX), M	5% MNX + 0.25% FNS, 0.25% FNS, or 5% MNX; 24 weeks	Higher hair density at 3 and 6 months with FNS + MNX but no difference in hair diameter. *No significant differences in hormone levels.*
Randomized double-blind trial, N=53, n= 19, M	0.25% FNS + 3% MNX or 3% MNX; 24 weeks	Significant increase in hair density, diameter, and global photo assessment with FNS + MNX. *Minimal effect on plasma DHT levels.*
Randomized single-blind trial, N=164, n = 82, M	0.25% FNS + 5% MNX or 5% MNX; 12 weeks	Over 80% of FNS + MNX vs 69.1% of MNX had improvement in SALT* score.
Randomized single-blind trial, N=50, n = 25, M	5% MNX + 0.1% FNS or PRP + 5% MNX + 0.1% FNS; 25 weeks	PRP group had non-statistically significant greater improvement.
Retrospective cohort, N=50, n = 50, M	5% MNX + 0.1% FNS; 52 weeks	25 patients maintained moderate density; 13 improved, 7 declined.
Retrospective cross-sectional, N=238, n = 238, M	0.1% FNS + 3% MNX; 6 weeks	62.2% of patients reported positive changes in hair appearance; 44.1% reported improved self-esteem.
Randomized double-blind trial, N=30, n = 15, F	0.25% FNS + 3% MNX or 3% MNX; 24 weeks	Improved hair density and diameter by 24 weeks (greater in FNS + MNX). *Significant decrease in serum DHT levels in combination topical.*
Randomized double-blind trial, N=40, n = 17, M	3% MNX or 3% MNX + 0.1% FNS; 24 weeks	MNX + FNS group with greater improvement on photographic assessment but hair counts not statistically different between groups.
Case series, N=5, n = 5, M	10% MNX, 0.1% FNS, 0.2% biotin, 0.05% caffeine citrate; 24 weeks	Photo assessment with increase in hair density.
Randomized double-blind trial, N=60, n = 40 (20 FNS, 20 FNS + MNX), M	5% MNX, 0.25% FNS, or 5% MNX + 0.25% FNS; 24 weeks	Terminal hair density improved across all groups at 12 weeks. FNS + MNX with significantly greater increase in hair density at 24 weeks.
Randomized double-blind trial, N=34, n = 17, F	MN + 0.01% DTS or MN + saline; 20 weeks	MN + DTS improved hair thickness, density, and vellus/terminal hair ratio.
Randomized double-blind trial, N=30, n =10, M&F	5% MNX, 5 MNX + 0.02% DTS + MN, or 0.5mg oral DTS; 16 weeks	DTS + MN and oral DTS with greatest benefit in hair density and caliber. MN had fewer systemic side effects.

Abbreviations: DTS: dutasteride, FNS: finasteride, MN: microneedling, MNX: minoxidil

using the 2009 Oxford Levels of Evidence, available via Mendeley at https://data.mendeley.com/datasets/fdjwx97hwt/1 (Supplementary Table 1).

The 19 articles featured 1632 participants, with 874 receiving treatment with topical 5-ARIs. Although there was no standard method of reporting age amongst included studies, all reports featured adult participants. Tables 1 and 2 outline demographics and clinical characteristics of patients who underwent treatment with topical 5-ARIs. Eight studies investigated the effects of topical 5-ARIs alone (Table 1), 2 investigated alternative delivery methods such as microneedling (Table 2), and 10 investigated topical 5-ARIs in combination with other additives such as minoxidil (Table 2), with one study exploring topical 5-ARIs as both a monotherapy and in combination with minoxidil. Topical 5-ARIs included finasteride (n=16 studies), alfatradiol (n=1), and dutasteride (n=2).

Of the 19 studies, 14 studies showed a significant improvement in the severity of AGA following treatment with topical 5-ARIs. Improvement was measured through various metrics such as hair density, photographic assessment, and patient and clinician assessment (Tables 1 and 2). The mean follow-up time was 27.2 months, with some studies noting improvement in hair density as early as month 2.[2] When stratified by formulation, topical 5-ARIS used in combination with other medications, such as minoxidil, were more effective at inducing hair growth than topical 5-ARIs alone (Tables 1 and 2). Interestingly, some studies showed significantly less serum DHT inhibition for topical 5-ARIs compared to oral 5-ARIs, while others showed similar levels of serum DHT inhibition (Tables 1 and 2). Topical 5-ARIs were generally well tolerated, with the most common reported side effects being pruritus, dryness, and scaling. Prior studies, including a pharmacovigilance study and a systematic review with meta-analysis, have also shown that topical 5-ARIs are well-tolerated.[3,4]

Overall, topical 5-ARIs appear to have efficacy in treating AGA, but the extent to which they limit serum DHT inhibition (as compared to oral 5-ARIs) remains unclear. Limitations of our review include heterogeneity of metrics used to assess treatment response as well as unreported changes in serum DHT concentration in numerous studies. Further studies are needed to more definitively assess the efficacy and safety of topical 5-ARIs in the treatment of AGA.[3,4]

DISCLOSURES

The authors have no conflicts of interest to disclose.

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