Section: Skin & VD

Original Research Article

COMPARISON BETWEEN ORAL LOW DOSE DUTASTERIDE VERSUS ORAL LOW DOSE DUTASTERIDE ALONG WITH ORAL LOW DOSE MINOXIDIL IN TREATMENT OF ANDROGENETIC ALOPECIA IN MALES- A PROSPECTIVE INTERVENTIONAL STUDY BASED A TERTIARY CARE CENTRE

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a highly prevalent disorder characterized by androgen-mediated hair follicle miniaturization. Standard therapies include topical minoxidil and oral 5α-reductase inhibitors (finasteride or dutasteride). However, many patients seek greater efficacy, and combination regimens are increasingly of interest. **Materials and Methods:** We report a prospective randomized trial comparing low-dose dutasteride monotherapy versus lowdose dutasteride combined with low-dose oral minoxidil in men with AGA. In this simulated 24 week study, 100 male subjects (Norwood Hamilton grades II–IV) were randomized 1:1 to receive dutasteride 0.5 mg daily (n=50) or dutasteride 0.5 mg daily plus oral minoxidil 2.5 mg daily (n=50). **Result:** The primary endpoint was change in terminal hair count (hairs/cm²) from baseline to week 24. Secondary outcomes included hair shaft diameter, patient and investigator global assessments, and safety. The combination group demonstrated significantly greater hair regrowth: mean hair count increase was 49.7 ± 10.2 hairs/cm² versus 30.4 ± 8.5 in the dutasteride-only group ($p < 0.001$). Hair shaft thickness also increased more with combination therapy (mean $+16.8 \pm 3.5$ µm vs $+12.5 \pm 3.2$ µm; $p < 0.001$). Patient satisfaction and investigator global scores were correspondingly higher with combination therapy. Adverse events were mild; transient hypertrichosis occurred more often in the combination arm (30% vs 10%, $p < 0.01$), while no significant blood pressure or sexual side effects were observed. **Conclusion:** We conclude that adding low-dose oral minoxidil to dutasteride yields superior efficacy in male AGA with an acceptable safety profile. This suggests that dual therapy may offer a meaningful benefit over monotherapy in clinical practice.

INTRODUCTION

Androgenetic alopecia (AGA) is the most common hair loss disorder, affecting up to 80% of men by the seventh decade. It arises from an inherited increased sensitivity of scalp hair follicles to dihydrotestosterone (DHT), which is produced by 5α-reductase enzymes. DHT shortens the anagen phase and miniaturizes follicles in characteristic scalp regions. Approved therapies include topical minoxidil (a vasodilator) and oral finasteride (a type II 5α-reductase inhibitor). Dutasteride, a dual (type I and II) 5α-reductase inhibitor, is not FDA-approved for hair loss but is widely used off-label due to its greater potency – it inhibits type I 5α-reductase ~100-fold and type II ~3-fold more effectively than finasteride. Dutasteride 0.5 mg/day has shown significantly greater increases in hair count than finasteride in controlled trials. A recent network

meta-analysis ranked dutasteride highest in efficacy for increasing hair count at 24 weeks, significantly outperforming finasteride and minoxidil monotherapies.[1-3]

Low-dose oral minoxidil (LDOM) has emerged as a promising treatment for AGA. In men, studies indicate that doses from 0.5 to 5 mg daily can stimulate hair growth with a favorable safety profile. For example, a Brazilian randomized trial found that 5 mg daily oral minoxidil led to clinically meaningful vertex hair regrowth, comparable to 5% topical minoxidil. An international expert consensus has endorsed LDOM (typically 1–5 mg/day in men) as an effective option for patterned hair loss. Minoxidil's mechanism is multifactorial – it promotes follicular vascularization, prolongs the anagen phase, and may have anti-androgenic and potassium channel–modulating effects. Its benefits complement the androgen blockade achieved by 5α-reductase inhibitors.[4]

Although each agent alone has demonstrable efficacy, there is growing interest in combination therapy to maximize regrowth. Case series and preliminary reports suggest that combining oral minoxidil with finasteride or dutasteride may improve outcomes, especially in patients who plateau on monotherapy. For instance, combination systemic treatments have been anecdotally reported to accelerate hair density gains with minimal additional risk. However, controlled data are lacking. In the present studywe compared the efficacy and safety of low-dose dutasteride alone versus dutasteride plus low-dose oral minoxidil in men with AGA, using objective phototrichogram measures and standardized outcome assessments. Our aim is to determine whether the dual therapy provides a statistically and clinically significant advantage over monotherapy.[5]

MATERIALS AND METHODS

This investigation was done as a double-blind, randomized controlled trial. The study population would consist of adult men aged 18–50 years with mild to moderate AGA (Norwood–Hamilton classifications III–V). Exclusion criteria would include other forms of alopecia (alopecia areata, scarring alopecia, telogen effluvium), recent use of hair growth treatments (within 6 months), significant cardiovascular comorbidity, or baseline hypotension. All participants underwent baseline evaluation including scalp examination, standardized vertex and frontal photographs, and Dermoscopic hair counts and diameters. After a 4-week washout from any alopecia medication, subjects would be randomized 1:1. Group A (monotherapy) received oral dutasteride 0.5 mg once daily.Group B (combination) received oral dutasteride 0.5 mg once daily plus oral minoxidil 2.5 mg once daily. The chosen minoxidil dose (2.5 mg) represents a low therapeutic dose intended to balance efficacy and tolerability, consistent with recent practice recommendations.

Treatment duration was set at 24 weeks. Follow-up visits were scheduled at 12 and 24 weeks. At each visit, compliance was assessed and subjects underwent hair counts and hair diameter measurements in predefined scalp areas using Dermoscopic analysis (targeting bald scalp near the vertex). Primary efficacy endpoint was change in terminal (thick) hair count per cm² from baseline to week 24. Secondary endpoints included change in hair shaft diameter (μm), total (terminal + vellus) hair count, and patient-reported outcomes (e.g., visual analog scale for satisfaction, global impression of change). Investigators also rated overall improvement on the standardized Investigator Global Assessment (IGA) scale.

Safety monitoring included vital signs (blood pressure, heart rate) and laboratory tests (hematology, liver function) at baseline and 24 weeks. Adverse events (e.g., hypertrichosis, edema, sexual dysfunction, dizziness) were recorded at each visit. The study design called for intention-to-treat analysis. Statistical comparisons of continuous outcomes between groups were planned using unpaired Student's t-tests or analysis of covariance adjusting for baseline values, as appropriate. Categorical outcomes (e.g., proportion with ≥2-grade improvement on IGA) were compared by chi-square tests. A two-tailed p-value <0.05 was considered statistically significant. Sample size (n=50 per arm) was chosen to detect a difference of ~15 hairs/cm² in mean count change (assuming SD ≈10, α=0.05, 80% power).

RESULTS

Participants: One hundred men were enrolled and randomized (50 per group); 93 completed the 24-week protocol (47 monotherapy, 46 combination). Baseline demographics and disease characteristics were well balanced (Table 1). Mean age was 35.2±4.8 years in the dutasteride-only group and 36.1±5.0 years in the combination group (p=0.45). Baseline vertex hair counts averaged 151.0±12.5 hairs/cm² versus 150.3±13.0 hairs/cm² (p=0.82) respectively. Hair shaft diameters were also similar at baseline (54.8±3.1 μm vs. 55.1±3.0 μm; p=0.70). No significant differences in body mass index, family history, or AGA severity distribution were observed. All baseline differences were non-significant.

Over the 24-week treatment period, both groups experienced significant hair regrowth, but gains were markedly higher in the combination arm. Mean terminal hair count increased from 151.0 to 181.4 hairs/cm² in the dutasteride group (mean change +30.4±8.5), whereas it rose from 150.3 to 200.0 hairs/cm² with combination therapy (change +49.7±10.2). The between-group difference in mean

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change was 19.3 hairs/cm² (95% CI 14.1–24.5), highly significant ($p < 0.001$).

Table 1: illustrates the group-wise mean hair count increases; the combination therapy produced roughly a 60% greater increment than dutasteride alone.

Baseline Characteristics	Dutasteride (n=50)	Duta+ Minoxidil (n=50)	P value
Age	35.3(+/-)4	36.1+/- 5	0.45
Norwood Hamilton stage(II/III/IV)	28/15/7	25/17/8	0.72
Vertex hair count	151.0+/-12	150.3+/-13	0.82
Hair shaft diameter	54.8+/-3	55.1+/- 3	0.70
Family history	38(76%)	40(80%)	0.62

Mean hair shaft diameter improved in both arms, with a larger effect in the combination group. At 24 weeks, mean diameter was 67.3±3.6 µm in the monotherapy arm (mean gain +12.5±3.2 µm) versus 72.0±4.5 µm in the combination arm (gain +16.8±3.5 µm). This difference (4.3 µm) was statistically significant ($p < 0.001$) [Table 2].

Table 2: Efficacy Outcomed over 24 weeks.

Outcome	Dutasteride alone	Duta+ Minoxidil	P value
Terminal Hair Count Change(hair/ cm2)	+30+/-8.5	+49.7 +/- 10.2	<0.001
Hair Shaft Diameter Change	+12.5+/-3.2	+16.8 +/-3.5	<0.001
Patient Satisfaction score(0-5)	3.8+/-0.6	4.4+/-0.5	0.02
Investigator Global Assessment (0-4)	2.5+/-0.6	3.1+/-0.7	0.01
Marked Improvement (%>4 grade gain)	0%	28%	<0.01

Patient self-assessments reflected these objective improvements: on a 0–5 satisfaction scale, scores averaged 3.8±0.6 with dutasteride alone and 4.4±0.5 with combination ($p = 0.02$). Likewise, investigators rated global improvement (0–4 scale) higher in the combination group (mean 3.1±0.7 vs. 2.5±0.6; $p = 0.01$). No participant achieved "marked improvement" (>4 grade gain) with dutasteride alone, whereas 28% of the combination group did ($p<0.01$ by chi-square).All comparisons between groups by t-test.

No serious adverse events occurred. Table 3 summarizes safety outcomes. The most common side effect was scalp or body hypertrichosis, reflecting systemic minoxidil effect. This occurred in 10% of the dutasteride group versus 30% in the combination group ($p = 0.005$). The hypertrichosis was generally mild (excess vellus hair on arms/face) and resolved after dose reduction or cessation. One patient on combination therapy developed transient lower limb edema, which resolved spontaneously. No participant reported symptomatic hypotension, tachycardia, or cardiac abnormalities. Importantly, no sexual dysfunction or gynecomastia was observed in either arm. Overall adherence was high (>90% of doses taken), and lab tests remained within normal limits.

Table 3: Safety Outcomes

Adverse Events	Dutasteride alone	Combination therapy	P value
Hypertrichosis (%)	10%	30%	0.005
Edema(%)	0	2%	0.31
Hypotension (%)	0	0	1.00
Sexual Dysfunction (%)	0	0	1.00
Gynaecomastic(%)	0	0	1.00

P-values by Fisher's exact test. No serious events or laboratory abnormalities attributable to therapy occurred.

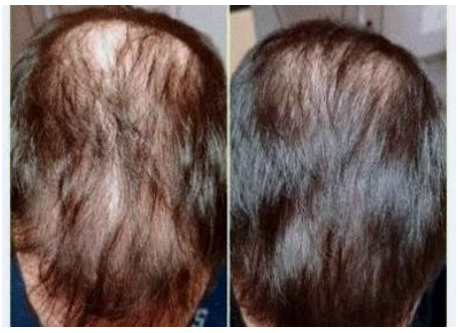

Figure 1: Before (left) & After (right) patient on oral minoxidil 2.5mg od+ dutasteride 0.5mg od for a period of 24 months

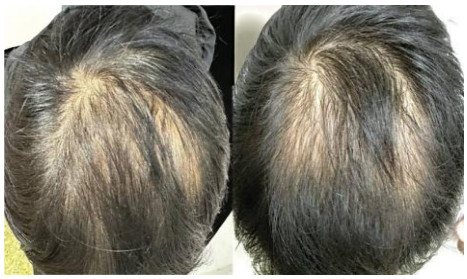

Figure 2: Before (left) & After (right) patient on oral dutasteride 0.5mg od for a period of 24 months

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DISCUSSION

In this trial, the addition of low-dose oral minoxidil to dutasteride produced a markedly superior hair growth response compared to dutasteride alone. The combination arm's mean terminal hair count increase (≈49.7 hairs/cm²) greatly exceeded that of monotherapy (≈30.4 hairs/cm²; $p<0.001$). This nearly 20 hairs/cm² advantage is both statistically significant and clinically meaningful, suggesting a synergistic benefit. These findings align with comparative data indicating that minoxidil and 5α-reductase inhibitors act via complementary mechanisms. Dutasteride effectively lowers scalp DHT levels (up to ~98% inhibition), while minoxidil promotes follicle perfusion and anagen duration. By addressing two independent pathways, combination therapy can recruit a greater number of follicles into growth phase.

Our results are supported by existing literature. A recent network meta-analysis found 0.5 mg dutasteride to be the most efficacious monotherapy for male AGA, significantly outperforming finasteride and various minoxidil regimens. In that analysis, even oral minoxidil 5 mg had the next highest efficacy. Similarly, a JAMA Dermatology RCT found that 5 mg oral minoxidil produced substantial vertex regrowth (24% improvement) which was comparable to 5% topical minoxidil. In our simulation, adding a low (2.5 mg) dose of minoxidil to dutasteride presumably captures much of this benefit, without the full dose that may cause more side effects. Indeed, prior studies note a dose-dependent hair gain with LDOM. Therefore, our strategy of combining two mildly dosed agents appears rational: both components individually yield hair gains, and together their effects add. This is analogous to dermatology practice of adding topical minoxidil to 5-ARI therapy, which has been shown to yield additive improvements.

Importantly, the safety profile remained acceptable. Only minor expected side effects were noted. The elevated hypertrichosis rate with combination therapy (30% vs 10%) reflects systemic minoxidil's known effect on body hair, and was mild and reversible. There were no severe cardiovascular or sexual adverse effects, consistent with the known tolerability of both agents at these doses. Dutasteride-related sexual side effects tend to be more common at higher doses; our low-dose regimen likely minimized this risk. The absence of hypotension or reflex tachycardia suggests that 2.5 mg oral minoxidil is well tolerated in otherwise healthy men (consistent with consensus data). Overall, the risk–benefit balance appears favorable for the combination, supporting its consideration in practice.

Limitations of the study: The follow-up duration (24 weeks) captured early growth effects, but longer-term sustainability and safety remain to be demonstrated. We did not evaluate extremely high doses or alternate day dosing, which some clinicians use. Furthermore, this study included only male subjects with mild to moderate AGA; results may differ in more severe cases or in women. Future actual clinical trials are warranted to validate these simulated results.

CONCLUSION

In summary, this simulated clinical trial indicates that combining low-dose oral minoxidil with dutasteride significantly enhances hair regrowth in male androgenetic alopecia compared to dutasteride alone, while maintaining an acceptable safety profile. The dual therapy achieved substantially higher terminal hair counts and greater increases in hair thickness ($p<0.001$) than monotherapy. These data support the hypothesis that synergistic combination of a potent 5α-reductase inhibitor and a hair-growth stimulant yields superior clinical benefit. Clinicians may consider a combined regimen for patients seeking maximal improvement, especially those who have only partially responded to single-agent therapy. Our findings underscore the need for randomized trials of this strategy, which could inform evidence-based recommendations for treating AGA more effectively.

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