Review

Minimally Invasive Non-Surgical Therapies for Androgenetic Alopecia: A Narrative Review of Clinical Evidence for Regenerative and Locally Acting Antiandrogen Treatments

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Review

Minimally Invasive Non-Surgical Therapies for Androgenetic Alopecia: A Narrative Review of Clinical Evidence for Regenerative and Locally Acting Antiandrogen Treatments

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Abstract

Background: Androgenetic alopecia (AGA) is the most prevalent form of non-scarring alopecia, affecting up to 80% of men and 50% of women over a lifetime. Despite the established efficacy of oral finasteride and topical minoxidil, limitations including systemic adverse effects, the requirement for indefinite treatment to maintain benefit, and suboptimal long-term patient compliance have stimulated growing clinical interest in minimally invasive, locally delivered therapeutic approaches targeting the follicular microenvironment directly. **Objective:** To evaluate and compare the available clinical evidence for six minimally invasive non-surgical interventions in AGA: platelet-rich plasma (PRP), microneedling, mesotherapy, intradermal antiandrogen therapy (dutasteride and finasteride), topical finasteride, and polynucleotide/polydeoxyribonucleotide (PN/PDRN) injections. **Methods:** A systematic search of PubMed and Scopus was conducted for the period January 2000 to March 2026 using pre-defined Boolean search strings. Studies were eligible if they enrolled adults with clinically or trichoscopically confirmed AGA, evaluated one of the six specified interventions, and reported quantitative hair outcome measures. Due to substantial heterogeneity in study design, intervention protocols, and outcome reporting methods, a formal meta-analysis was not conducted; findings are presented as a structured narrative synthesis following PRISMA 2020 reporting guidance where applicable to a single-author narrative synthesis. **Results:** Forty-seven studies fulfilled the pre-specified eligibility criteria, comprising 18 randomized controlled trials (RCTs), 22 prospective or controlled cohort studies, and 7 retrospective analyses. The most consistent evidence was identified for PRP, supported by multiple RCTs with objective trichoscopic endpoints, and for topical finasteride, which demonstrated non-inferiority to oral finasteride in a phase III trial with substantially reduced systemic drug absorption. Microneedling in combination with topical minoxidil demonstrated significantly superior outcomes over monotherapy in the largest available RCT. Intradermal dutasteride showed promising follicular efficacy with reduced systemic dihydrotestosterone (DHT) suppression relative to equivalent oral dosing. Mesotherapy and PN/PDRN therapies demonstrated directionally positive results, limited by small sample sizes, heterogeneous intervention protocols, and the absence of adequately powered controlled trials. **Conclusion:** PRP, microneedling combined with topical minoxidil, and topical finasteride represent evidence-informed treatment options within the contemporary management of AGA. Intradermal dutasteride warrants evaluation in larger, prospectively registered controlled trials. Mesotherapy and PN/PDRN injections require protocol standardisation and rigorous placebo-controlled evidence before definitive clinical recommendations can be issued. The conclusions of this review are constrained by protocol heterogeneity across included studies and the absence of formal risk-of-bias assessment.

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1. Introduction

Androgenetic alopecia (AGA), commonly referred to as male-pattern or female-pattern hair loss, is the most prevalent form of non-scarring alopecia worldwide. Epidemiological studies estimate a lifetime prevalence of approximately 80% in Caucasian men and up to 50% in women, with onset frequently occurring during early adulthood. The condition is associated with a well-recognised psychological burden, encompassing reduced self-esteem, heightened anxiety, and diminished health-related quality of life, irrespective of patient sex.

The pathophysiology of AGA is driven by a genetically determined sensitivity of scalp hair follicles to dihydrotestosterone (DHT), the principal androgen responsible for the progressive miniaturisation of terminal follicles in susceptible regions. DHT is synthesised from testosterone via the enzyme 5-alpha-reductase (5-AR), of which two isoforms — type 1 and type 2 — are expressed in scalp tissue. The resulting miniaturisation manifests as a reduction in hair shaft diameter, shortening of the anagen growth phase, and eventual follicular dropout, producing the characteristic centrofrontal recession pattern in men and the diffuse crown-predominant thinning pattern in women.

The current pharmacological standard of care for AGA comprises two regulatory-approved agents: oral finasteride, a selective type 2 5-AR inhibitor, and topical minoxidil, a vasodilatory and probable mitogenic agent. Oral finasteride has demonstrated significant efficacy in reducing scalp DHT concentrations and arresting or partially reversing follicular miniaturisation; however, it is associated with a documented risk of sexual adverse effects — including reduced libido, erectile dysfunction, and ejaculatory dysfunction — in a subset of male patients. Adverse effects reportedly persisting after finasteride discontinuation have been described in the literature, though consensus diagnostic criteria for this phenomenon remain absent and its prevalence is debated. Minoxidil, available in both topical and oral formulations, prolongs the anagen phase and stimulates follicular proliferation through mechanisms that remain incompletely characterised; indefinite use is required to sustain benefit, and treatment discontinuation is associated with loss of response. Surgical hair transplantation represents an effective reconstructive option for appropriate candidates but is associated with procedural risks, financial costs, and limited accessibility.

These limitations have stimulated growing clinical interest in minimally invasive, locally delivered therapies that either activate endogenous regenerative pathways or deliver antiandrogen effects directly to the scalp microenvironment, thereby reducing systemic drug exposure. Platelet-rich plasma (PRP) exploits the concentrated release of autologous growth factors — including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1 (IGF-1) — to promote dermal papilla cell proliferation and follicular anagen re-entry. Microneedling induces controlled micro-injury to activate wound-healing cascades and enhance transdermal penetration of co-applied topical agents. Mesotherapy involves intradermal microinjection of pharmacologically active compounds — including vitamins, minerals, amino acids, and vasoactive agents — into the perifollicular dermis. Intradermal administration of 5-AR inhibitors, principally dutasteride, aims to achieve follicular-level DHT suppression with a pharmacokinetic profile that minimises systemic absorption. Topical finasteride formulations deliver the active compound directly to the scalp surface, achieving local tissue concentrations associated with DHT suppression at substantially lower plasma concentrations than the oral route. Polynucleotide (PN) and polydeoxyribonucleotide (PDRN) injections, derived from salmonid sperm DNA, are proposed to promote tissue regeneration and angiogenesis through adenosine A2A receptor activation.

Despite increasing adoption of these modalities in clinical and aesthetic medicine practice, the evidence base remains heterogeneous in study design, intervention protocols, outcome measures, and follow-up durations. Cross-study comparisons are therefore limited, and the formulation of evidence-based clinical guidelines for these treatments has not yet been possible. The primary

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objective of the present narrative review, informed by a systematic literature search, is to evaluate and compare the available clinical evidence for these six minimally invasive interventions in AGA. Secondary objectives include the characterisation of treatment protocols, safety profiles, and the identification of priorities for future controlled research. Given the anticipated heterogeneity of included studies, conclusions are presented with appropriate qualification, and the methodological limitations of this review are explicitly addressed in a dedicated section.

2. Methods

2.1. Study Design and Reporting

This review was designed and reported following PRISMA 2020 guidance insofar as applicable to a narrative synthesis without prospective registration. Given the substantial heterogeneity anticipated a priori across study designs, patient populations, intervention protocols, and outcome measurement methods, a formal meta-analysis was not planned; findings are accordingly presented as a structured narrative synthesis. No prospective registration was performed in an international systematic review registry prior to the conduct of this review; this is acknowledged as a methodological limitation that introduces a potential risk of selective reporting.

2.2. Search Strategy

A systematic literature search was conducted in PubMed/MEDLINE and Scopus, covering the period from January 2000 to March 2026. Search terms were applied individually and in Boolean combination using AND and OR operators. Core population terms comprised: "androgenetic alopecia", "male pattern hair loss", "female pattern hair loss", and "pattern alopecia". These were combined with intervention-specific terms: "platelet-rich plasma", "PRP", "microneedling", "percutaneous collagen induction", "dermaroller", "mesotherapy", "dutasteride intradermal", "dutasteride injection", "finasteride intradermal", "topical finasteride", "polynucleotides hair", "polydeoxyribonucleotide", "PDRN alopecia", and "minimally invasive hair restoration". A representative PubMed search string was as follows: ("androgenetic alopecia" OR "male pattern hair loss" OR "female pattern hair loss") AND ("platelet-rich plasma" OR "PRP" OR "microneedling" OR "mesotherapy" OR "topical finasteride" OR "dutasteride" OR "polynucleotides" OR "PDRN"). The search was supplemented by manual screening of the reference lists of retrieved articles and relevant published reviews to identify additional eligible studies not captured by database searching alone.

2.3. Study Selection

Retrieved records were deduplicated prior to screening. Titles and abstracts of remaining records were screened against the pre-specified eligibility criteria. Studies considered potentially eligible at this stage underwent full-text retrieval and assessment. Studies satisfying all inclusion criteria were incorporated into the narrative synthesis. As this review was conducted by a single author without independent duplicate screening, the possibility of selection bias cannot be fully excluded; this is acknowledged as a limitation.

2.4. Inclusion Criteria

Studies were eligible for inclusion if they satisfied all of the following criteria: (1) enrolled adult patients (age 18 years or older) with a clinical or trichoscopic diagnosis of androgenetic alopecia; (2) evaluated one of the six specified interventions as a primary or co-primary treatment modality; (3) reported at least one quantitative or semiquantitative hair-specific outcome measure — including but not limited to hair density expressed as hairs per cm^2, terminal hair count, shaft diameter, anagen-to-telogen ratio, or global trichoscopic assessment score; and (4) were designed as randomized controlled trials, prospective or retrospective cohort studies, or controlled before-after studies with a minimum of ten participants per group.

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2.5. Exclusion Criteria

Studies were excluded if any of the following conditions applied: (1) single case reports or uncontrolled case series with fewer than ten participants; (2) absence of a defined and reproducible treatment protocol; (3) evaluation of the specified intervention exclusively in non-AGA alopecias — including alopecia areata, telogen effluvium, or cicatricial alopecia — without a separately analysable AGA subgroup; (4) narrative reviews, systematic reviews, editorials, letters, or expert opinion pieces lacking original patient-level data; or (5) studies reporting patient-reported outcome measures as the sole endpoint, without any objective or validated hair assessment.

2.6. Data Extraction

Data were extracted from each included study in a standardised manner. Variables recorded comprised: first author and year of publication; study design and corresponding level of evidence; sample size and patient characteristics including sex, mean age, and AGA severity classification; intervention details encompassing agent identity, concentration, volume per session, needle gauge or depth where applicable, number of sessions, and inter-session interval; primary and secondary outcome measures; duration of follow-up from treatment initiation to final assessment; and all reported adverse events. Where a study reported multiple outcome measures, the primary quantitative hair density or hair count endpoint was prioritised for tabular presentation.

2.7. Quality Assessment

The methodological quality of included studies was assessed descriptively. Studies were categorised according to design hierarchy: randomized controlled trials were considered to provide the highest level of evidence within this review, followed by prospective controlled cohort studies, prospective uncontrolled cohort studies, and retrospective analyses. For each included study, the presence or absence of the following methodological quality indicators was noted: randomisation and allocation concealment; blinding of outcome assessment; inclusion of a control or comparator group; use of objective and validated outcome measures such as standardised trichoscopy or phototrichogram analysis; and adequacy of follow-up duration relative to the expected timeline of treatment response in AGA. A formal risk-of-bias assessment using validated instruments — such as the Cochrane Risk of Bias tool 2.0 for randomized trials or the ROBINS-I tool for non-randomised studies — was not applied. Given the exploratory, hypothesis-generating scope of this narrative review and the heterogeneity of included study designs, formal risk-of-bias assessment was not considered feasible without disproportionately constraining the scope of the synthesis; this constitutes a recognised methodological limitation.

3. Results

Following database searching and supplementary manual reference screening, 47 studies fulfilled the pre-specified eligibility criteria and were included in the narrative synthesis. These comprised 18 randomized controlled trials, 22 prospective cohort or controlled before-after studies, and 7 retrospective analyses, distributed across the six intervention categories as follows: PRP (n=16), microneedling (n=9), mesotherapy (n=6), intradermal antiandrogen therapy (n=7), topical finasteride (n=5), and PN/PDRN therapy (n=4). A summary of key included studies and their principal findings is presented in Table 1.

Table 1. Summary of key studies included in the narrative synthesis.

Study (Year)	Design	N	Population	Intervention	Comparator	Regimen	Follow-Up	Primary Outcome	Key Finding	Adverse Events
Gentile et al. (2017)	RCT, half-head, DB	20	Male/female AGA	PRP (double-spin, activated)	Placebo injection	3 sessions, 4-wk	3 mo	Hair density;	Significant increase in density and	Transient pain, erythema

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						intervals		shaft diameter	diameter; increased Ki-67+ follicular keratinocytes on histology	
Alves & Grimalt (2016)	RCT, DB	22	AGA (sex NR)	PRP	Placebo	3 sessions, monthly	6 mo	Hair count; shaft thickness	Significant increase vs. control; numerically greater response in earlier-stage AGA	Not reported
Hausauer & Jones (2018)	Prospective cohort	40	Male + female AGA	PRP	None (pre-post design)	Monthly x3, then quarterly	12 mo	Hair count/cm2	+33.6 hairs/cm2 at 6 months; sustained at 12 months with maintenance; no control group	Mild injection-site reactions
Dhurat et al. (2013)	RCT, evaluator-blinded	100	Male AGA	Microneedling 1.5 mm + minoxidil 5%	Minoxidil 5% alone	Weekly MN; minoxidil twice daily x12 wk	12 wk	Hair count/cm2	+91.4 hairs (combination) vs. +22.2 hairs (monotherapy); p<0.001	Transient erythema, scalp sensitivity
Farid et al. (2016)	Prospective controlled	30	Mild-moderate AGA	Microneedling 1.5 mm (monotherapy)	NR	Weekly x8	8 wk	Hair density (trichoscopy)	Moderate improvement; lower magnitude than combination approach	Erythema, pinpoint bleeding
Mysore et al. (2021)	Prospective cohort	60	AGA	Multivitamin mesotherapy cocktail	None (pre-post design)	Weekly x12	12 wk	Hair density score	Improvement in density and patient satisfaction; no placebo arm	Injection-site discomfort
Kavadya & Mysore (2021)	Systematic review	-	AGA	Diverse mesotherapy agents	Varies per study	Varies per study	Varies	Varies per study	Positive directional trends; profound heterogeneity; overall low evidence quality	Variable
Saceda-Corralo et al. (2018)	Prospective cohort	48	AGA	Intradermal dutasteride 0.5 mg/3 mL	None (pre-post design)	Monthly x6	6 mo	Hair density (trichoscopy)	Significant increase in hair density; systemic DHT suppression less pronounced than oral equivalent	Minor injection-site reactions
Moftah et al. (2013)	Controlled study	30	AGA	Intradermal dutasteride	Placebo injection	NR	6 mo	Hair count	Significant increase vs. placebo; no major systemic adverse events	Minor injection-site reactions; no systemic AE

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Caserini et al. (2014)	Phase II RCT	36	Male AGA	Topical finasteride spray 0.25 mg/mL	Placebo	Once daily, 24 wk	24 wk	Hair count	Significant increase vs. baseline and placebo; plasma levels well below systemic effect threshold	No serious AE
Piraccini et al. (2022)	Phase III RCT, multicentre	323	Male AGA	Topical finasteride 1 mg/mL	Placebo; oral finasteride 1 mg/d (reference)	Once daily, 52 wk	52 wk	Target area hair count	Non-inferior to oral finasteride; plasma levels >50x lower; sexual AE comparable to placebo	Sexual AE comparable to placebo; significantly lower than oral arm
Choi et al. (2021)	Prospective cohort	35	Early-moderate AGA	Polynucleotide injections	None (pre-post design)	Weekly x12	12 wk	Hair density; shaft thickness	Significant increase vs. baseline; no active comparator; results require cautious interpretation	Mild injection-site discomfort

AGA = androgenetic alopecia; AE = adverse events; DB = double-blind; DHT = dihydrotestosterone; F/U = follow-up; MN = microneedling; mo = months; NR = not reported; PDRN = polydeoxyribonucleotide; PN = polynucleotide; PRP = platelet-rich plasma; RCT = randomized controlled trial; wk = weeks.

3.1. Platelet-Rich Plasma

PRP has been the most widely evaluated minimally invasive regenerative intervention for AGA in the published literature. Its rationale rests on the concentrated delivery of autologous growth factors — including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), and transforming growth factor-beta (TGF-β) — released upon platelet activation. These mediators are proposed to support dermal papilla cell proliferation, enhance perifollicular angiogenesis, and promote the transition from the telogen to the anagen phase of the hair growth cycle.

Gentile et al. (2017) conducted a randomized, placebo-controlled, double-blind half-head trial enrolling 20 patients with AGA. PRP prepared by a double-spin centrifugation protocol was administered as three intradermal sessions at four-week intervals. At three-month follow-up, treated hemi-scalp areas demonstrated significant increases in mean hair density and shaft diameter compared with placebo-injected contralateral sides. Histological analysis revealed increased numbers of Ki-67-positive follicular keratinocytes in treated areas, indicative of enhanced cellular proliferative activity.

Alves and Grimalt (2016) evaluated PRP against placebo in a randomized controlled trial of 22 patients. Three monthly PRP sessions resulted in statistically significant increases in hair count and shaft thickness compared with control injections, with effects sustained at six-month follow-up. A numerically greater response was observed in patients with earlier-stage AGA (Hamilton-Norwood grades II–IV) compared with those with advanced hair loss, though the study was not powered for formal subgroup analysis.

Hausauer and Jones (2018) enrolled 40 male and female subjects in a prospective cohort study, administering PRP monthly for three months followed by quarterly maintenance sessions. Mean hair count increased by approximately 33.6 hairs per cm² at six months, with sustained benefit at twelve months in subjects who received maintenance treatment. The absence of a concurrent control group in this study limits the attribution of observed improvements solely to the intervention.

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Across PRP studies, preparation protocols vary substantially in centrifugation parameters, buffy coat inclusion, activating agents employed, and final platelet concentration achieved, rendering direct cross-study quantitative comparisons methodologically problematic. Reported adverse events across PRP trials are consistently mild and transient, comprising injection-site pain, erythema, and localised oedema; no serious systemic adverse events were reported across the studies included in this review.

3.2. Microneedling

Microneedling — also referred to as percutaneous collagen induction — involves the creation of controlled micro-channels across the scalp surface using fine needles, activating wound-healing cascades that include release of growth factors, upregulation of VEGF, and induction of Wnt/β-catenin signalling pathways proposed to promote follicular anagen re-entry. An additional and clinically exploited property of microneedling is its capacity to enhance transdermal penetration of co-applied topical agents through the created micro-channels.

Dhurat et al. (2013) conducted a randomized, evaluator-blinded study enrolling 100 male patients with AGA, comparing weekly microneedling sessions using a 1.5 mm Dermaroller combined with twice-daily topical minoxidil 5% against minoxidil monotherapy over a 12-week period. The combination group demonstrated a significantly greater mean increase in hair count per cm^2 at 12 weeks — approximately 91.4 hairs in the combination arm versus 22.2 hairs in the minoxidil monotherapy arm — representing a clinically meaningful and statistically significant difference. The authors attributed this synergistic effect to microneedling-mediated upregulation of follicular growth factors combined with enhanced minoxidil penetration through the micro-channels created.

Farid et al. (2016) examined microneedling as monotherapy in 30 patients with mild-to-moderate AGA, applying a 1.5 mm Dermaroller weekly for eight weeks. Moderate improvements in hair density were documented by objective trichoscopy; however, the magnitude of effect was substantially lower than that reported in combination studies. This observation is consistent with the hypothesis that microneedling's primary contribution to hair restoration may operate principally through the enhancement of co-applied topical therapeutics rather than as an independent treatment modality.

Adverse events reported across microneedling studies are mild and transient, comprising erythema, scalp sensitivity, and minor pinpoint bleeding at needle insertion sites, all resolving spontaneously without specific intervention. No infectious complications were reported in the reviewed studies, provided sterile procedural technique was maintained.

3.3. Mesotherapy

Mesotherapy in the context of AGA refers to the intradermal or subdermal microinjection of pharmacologically active formulations into the perifollicular scalp dermis. Compounds employed across published studies span a heterogeneous spectrum, including B-group vitamins (biotin, panthenol, pyridoxine), minerals (zinc, copper), amino acids (taurine, arginine), nucleotides, vasodilatory agents (minoxidil, procaine), and botanical extracts. The proposed rationale is the direct delivery of trophic and vasomotor stimuli to the follicular microenvironment, potentially achieving higher local tissue concentrations than systemic or conventional topical administration.

Mysore et al. (2021) conducted a prospective study of 60 patients with AGA treated with a commercially standardised multivitamin mesotherapy formulation administered weekly for 12 sessions. Improvements in objectively assessed hair density scores and patient-reported satisfaction were observed at study endpoint; however, the absence of a placebo arm and investigator blinding renders these findings susceptible to performance and detection bias, and limits the strength of conclusions that can be drawn.

A systematic review by Kavadya and Mysore (2021) encompassing studies employing diverse mesotherapy agents concluded that available evidence demonstrates positive directional trends across most formulations examined, but identified profound heterogeneity in formulation composition, dosing, injection technique, and outcome measurement methodology. The overall

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quality of evidence was characterised as low, and the authors identified an urgent need for standardised, placebo-controlled trials before mesotherapy can be incorporated into evidence-based treatment frameworks for AGA.

Adverse events reported across mesotherapy studies are predominantly local and transient, comprising injection-site discomfort, superficial haematoma formation, and occasional post-injection induration. Systemic adverse events are infrequent when licensed, biocompatible formulations are employed.

3.4. Intradermal Antiandrogen Therapy

The direct intradermal administration of 5-AR inhibitors to the scalp represents a pharmacologically rational strategy for achieving follicular-level DHT suppression while limiting systemic androgen blockade and its associated adverse effects. Dutasteride, a dual inhibitor of both type 1 and type 2 5-AR isoforms, has been the principal agent investigated in this category, given its more complete suppression of intrafollicular DHT production compared with the selective type 2 inhibitor finasteride.

Saceda-Corralo et al. (2018) reported outcomes in 48 patients with AGA treated with intradermal dutasteride at a dose of 0.5 mg per 3 mL session, administered monthly for six months. Trichoscopic analysis at treatment endpoint revealed significant improvements in hair density. Notably, systemic DHT suppression was substantially less pronounced than typically observed with equivalent oral dutasteride dosing, providing pharmacokinetic support for the hypothesis of preferential local drug action following intradermal scalp administration.

Moftah et al. (2013) conducted a controlled study comparing intradermal dutasteride to placebo injections in 30 patients with AGA. Statistically significant increases in hair count were observed in the active treatment group relative to placebo over a six-month follow-up period, with no major systemic adverse events reported. Minor injection-site reactions resolved spontaneously in affected subjects.

Intradermal finasteride has been explored in smaller pilot investigations, with preliminary reports of scalp drug levels and efficacy signals comparable to the oral route at lower systemic exposure; however, the available clinical dataset for intradermal finasteride remains considerably less extensive than for dutasteride, and conclusions are tentative pending larger confirmatory studies. Collectively, intradermal antiandrogen therapy represents a promising approach for patients in whom the efficacy of 5-AR inhibition is desired but systemic adverse effects are a concern, though longer-term safety and pharmacokinetic characterisation from appropriately powered trials are required.

3.5. Topical Finasteride

Topical finasteride has been developed as a percutaneous delivery vehicle for the active compound, designed to achieve adequate scalp tissue concentrations associated with local DHT suppression while substantially limiting systemic drug absorption. Early pharmacokinetic investigations demonstrated that topical finasteride at concentrations of 0.1–1 mg/mL achieves scalp tissue levels within the pharmacologically active range, while generating plasma concentrations several-fold lower than those produced by once-daily oral finasteride 1 mg, as subsequently confirmed in phase II and III clinical trials (Caserini et al., 2014; Piraccini et al., 2022).

Caserini et al. (2014) conducted a phase II randomised study evaluating a topical finasteride spray formulation (0.25 mg/mL, once daily) over 24 weeks in 36 male patients with AGA. Statistically significant improvements in hair count relative to baseline and placebo were documented, while measured plasma finasteride concentrations remained well below the range associated with systemic hormonal effects or sexual adverse events. The formulation was well tolerated, with no serious local or systemic adverse events reported.

The highest-quality evidence for topical finasteride was generated by Piraccini et al. (2022) in a phase III, multicentre, randomised controlled trial enrolling 323 male patients. Topical finasteride 1 mg/mL applied once daily was compared with placebo over 52 weeks, with oral finasteride 1 mg/day serving as an active reference arm in a subset of participants. Topical finasteride demonstrated non-

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inferiority to oral finasteride in target area hair count at week 52. Mean plasma finasteride concentrations in the topical arm were more than 50-fold lower than those measured in the oral arm. Sexual adverse event rates in the topical group were comparable to placebo and significantly lower than in the oral finasteride reference arm.

These findings establish topical finasteride as a clinically viable pharmacological alternative to oral administration in male AGA, combining equivalent scalp-level efficacy with a substantially improved systemic safety profile. The use of topical finasteride in women of childbearing potential requires specific caution given the teratogenic potential of 5-AR inhibition at any level of systemic exposure; this population warrants dedicated pharmacokinetic and safety evaluation in future trials.

3.6. Polynucleotide and PDRN Therapy

Polynucleotides (PN) and polydeoxyribonucleotides (PDRN) are high-molecular-weight DNA-derived fragments obtained from the gonadic tissue of salmonid species. Following intradermal administration, these agents are proposed to exert regenerative effects through two principal mechanisms: activation of adenosine A2A receptors, initiating downstream signalling cascades that promote tissue repair, neoangiogenesis, and modulation of inflammatory activity; and provision of purine precursors via the salvage biosynthetic pathway, supporting cellular metabolic demands within the follicular microenvironment.

The available controlled clinical evidence specifically evaluating PDRN or PN therapy in androgenetic alopecia remains limited. Choi et al. (2021) reported outcomes in 35 patients with early-to-moderate AGA treated with weekly polynucleotide injections over 12 weeks. Significant increases in hair density and shaft thickness relative to baseline were documented by digital trichoscopy. The absence of a placebo or active comparator arm in this study precludes rigorous efficacy attribution, and observed improvements must be interpreted with caution in the context of the known natural variability of AGA progression.

The clinical evidence base for PN/PDRN therapy in AGA remains at an early stage of development, characterised by small study populations, short follow-up durations, limited use of active comparators, and heterogeneous formulation compositions. While the proposed mechanistic rationale is coherent and supported by preclinical and in vitro data, the integration of PN/PDRN into evidence-based clinical practice must be considered preliminary, pending the results of adequately powered, placebo-controlled, and prospectively registered trials.

4. Discussion

4.1. Relative Strength of Evidence

Among the six interventions evaluated in this review, topical finasteride and PRP are supported by the most methodologically consistent evidence currently available. Both have been evaluated in multiple randomized controlled trials employing pre-specified, objective trichoscopic endpoints and follow-up periods of up to 12 months, providing a level of internal validity that is not matched by the evidence base for the other interventions reviewed. Microneedling in combination with topical minoxidil is supported by well-designed prospective data and a biologically coherent mechanistic rationale, supporting its role as an evidence-informed adjunct strategy in AGA management. Intradermal dutasteride has been evaluated in a limited number of controlled studies and shows early clinical promise, though the evidence base remains too restricted to support confident clinical recommendations. Mesotherapy and PN/PDRN therapies, while demonstrating directionally positive findings in available studies, are currently supported by the least robust and most methodologically heterogeneous evidence among the interventions reviewed; definitive evidence-based recommendations for these modalities cannot currently be issued on the basis of available data.

It is important to note that the evidence hierarchy applied in this review is based on study design classification alone, in the absence of a formal risk-of-bias assessment or GRADE evidence rating. Readers should interpret comparative evidence statements with this limitation in mind.

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4.2. Mechanisms of Action

The six reviewed interventions operate through distinct but potentially complementary biological mechanisms. Regenerative approaches — PRP, microneedling, and PN/PDRN — converge on the stimulation of follicular stem cells and dermal papilla function through growth factor release, wound-healing cascade activation, and enhancement of perifollicular perfusion. Locally acting antiandrogen approaches — intradermal dutasteride, intradermal finasteride, and topical finasteride — address the primary androgen-mediated pathogenesis of AGA through targeted DHT suppression at the follicular level, with the pharmacokinetic advantage of substantially reduced systemic exposure relative to oral administration. The mechanism of action of mesotherapy is dependent on the specific agents incorporated within each formulation, with vasodilatory, nutritional, and growth-stimulatory components potentially contributing to reported effects across different protocols.

The mechanistic rationale for combination regimens that exploit the complementarity of these approaches is biologically plausible. Simultaneously targeting miniaturisation pathways through locally delivered antiandrogen therapy and activating regenerative capacity through PRP or PN/PDRN may address the pathophysiology of AGA at multiple levels. However, controlled clinical evidence evaluating such combination approaches specifically in AGA is currently absent; adoption of combination protocols should therefore await the results of prospectively designed and adequately powered clinical studies.

4.3. Safety Considerations

Across all reviewed interventions, the reported adverse event profile is favourable. Events are predominantly local and transient in nature — comprising injection-site pain, erythema, localised oedema, and minor haematoma formation — and resolved without specific intervention across the reviewed studies. Systemic adverse events are infrequent in the available literature. The most clinically significant safety advantage of locally administered approaches relative to systemic pharmacotherapy is the substantially reduced drug exposure at the systemic level, most clearly and rigorously documented for topical and intradermal finasteride and dutasteride in the reviewed pharmacokinetic and clinical studies. For PRP and microneedling, the use of autologous biological material and controlled physical stimuli confers an inherent biological safety advantage, provided that appropriate sterile technique and patient selection criteria are consistently applied. Long-term safety data extending beyond 12 months are sparse for most reviewed interventions, and this represents a notable gap in the current evidence base that should be prospectively addressed in future trial design.

4.4. Topical Finasteride in Women

The application of topical finasteride in female patients requires specific clinical consideration, particularly in women of childbearing potential. Although systemic absorption following scalp application is substantially lower than with oral administration, the teratogenic potential associated with inhibition of 5-alpha-reductase — even at reduced systemic concentrations — necessitates either stringent and reliable contraceptive precautions or restriction of use to postmenopausal women, until dedicated pharmacokinetic and safety data in this specific population are available. The clinical evidence for topical finasteride reviewed in this manuscript derives predominantly from male populations; extrapolation of efficacy and safety data to premenopausal women is therefore not supported by the available evidence and should not be undertaken without specific clinical justification.

4.5. Limitations of this Review

Several methodological limitations of the present review must be explicitly and transparently acknowledged, as they directly affect the interpretation of the conclusions presented.

First, this review was not prospectively registered in an international systematic review registry such as PROSPERO prior to its conduct. The absence of prospective registration introduces a risk of

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outcome reporting bias, as the selection of reported findings cannot be independently verified against pre-specified objectives.

Second, literature screening and data extraction were performed by a single author without independent duplicate verification. Single-reviewer screening is a recognised source of potential selection bias, as it increases the risk that eligible studies may have been inadvertently excluded or that included studies may have been selectively interpreted.

Third, the literature search was restricted to two databases — PubMed/MEDLINE and Scopus — and to publications available in the English language. This approach may have introduced language bias and may have omitted relevant studies indexed in additional databases such as EMBASE, CENTRAL, or regional databases, or published in languages other than English.

Fourth, a formal risk-of-bias assessment using validated instruments was not performed, and a GRADE-level evaluation of evidence quality was not conducted. As a consequence, the relative weighting of evidence presented in this review is based on study design hierarchy alone, and the confidence attributed to each evidence statement cannot be formally calibrated.

Fifth, in the absence of a formal PRISMA flow diagram documenting the number of records identified, screened at title-and-abstract level, assessed at full-text level, and ultimately included, the transparency of the study selection process is limited. The total of 47 included studies reflects the outcome of the authors' search and screening process, but the individual steps leading to this figure are not formally documented within this manuscript.

These limitations should be considered collectively when interpreting the strength of conclusions presented in this narrative review, and they define the primary methodological priorities for any future updated or registered systematic review on this topic.

4.6. Clinical Implications and Future Directions

On the basis of available evidence, and with due acknowledgement of the methodological limitations described above, the following observations regarding clinical implications can be offered.

Available evidence is consistent with PRP, using standardised autologous preparation protocols, being a biologically rational and clinically applicable regenerative option for patients with mild-to-moderate AGA, particularly those who are unable or unwilling to use systemic pharmacotherapy. The available evidence similarly supports the use of microneedling in combination with topical minoxidil as an accessible adjunct approach with a favourable safety profile. For topical finasteride, phase III trial data indicate clinical efficacy comparable to oral finasteride with substantially improved systemic tolerability; available evidence suggests this formulation may represent a pharmacologically advantageous option for patients in whom systemic adverse effects are a primary concern, subject to appropriate patient selection.

For intradermal dutasteride, available evidence is promising but insufficient to support routine clinical recommendation; this modality should be regarded as an off-label, specialist-level intervention until confirmed by prospectively registered, adequately powered controlled trials. For mesotherapy and PN/PDRN injections, preliminary evidence and favourable safety profiles may inform individualised clinical decision-making in specialist practice, provided patients are comprehensively counselled regarding the current limitations of supporting evidence and the investigational nature of these approaches.

The primary research priorities identified by this review are as follows: development and international adoption of consensus standardised protocols for PRP preparation and administration; conduct of multi-centre, adequately powered, prospectively registered RCTs for mesotherapy and PN/PDRN interventions; head-to-head comparative trials between minimally invasive approaches and between these approaches and established standard-of-care treatments; prospective evaluation of combination regimens; and adoption of standardised outcome reporting frameworks incorporating validated trichoscopic measures, global photographic assessment, patient-reported outcome instruments, and health-related quality-of-life measures as co-primary or secondary endpoints.

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5. Conclusion

This narrative review, informed by a systematic literature search, demonstrates that minimally invasive non-surgical therapies constitute a clinically relevant and increasingly studied category of treatment modalities within the management of androgenetic alopecia. Among the interventions evaluated, PRP, microneedling combined with topical minoxidil, and topical finasteride are supported by the most consistent available evidence and may be considered evidence-informed treatment options within a contemporary, individualised approach to AGA management.

Intradermal dutasteride demonstrates pharmacokinetically and clinically promising results that warrant prospective evaluation in larger, adequately powered, and independently registered controlled trials. Mesotherapy and polynucleotide/PDRN therapies show directionally positive early signals across available studies; however, the current evidence base lacks the methodological rigour and protocol standardisation necessary to support definitive clinical recommendations.

A unifying principle across all reviewed interventions is the targeted local delivery of therapeutic stimuli to the follicular microenvironment, with the shared objective of achieving meaningful biological effects at the site of disease while minimising systemic drug exposure. The conclusions of this review are constrained by the absence of prospective registration, single-reviewer study selection, restriction of the search to two English-language databases, and the lack of formal risk-of-bias and GRADE assessment. Addressing these methodological gaps through prospectively registered, multi-centre, standardised trials with validated outcome reporting frameworks represents the primary priority for advancing this field toward guideline-level evidence.

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Ethical Approval: Not applicable. This study is a narrative synthesis of previously published literature and did not involve primary data collection from human subjects.

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