Clinical, Cosmetic and Investigational Dermatology

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REVIEW

Efficacy and Safety of Hormonal Therapies for Acne: A Narrative Review

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Background and Objectives: Acne vulgaris is a common inflammatory skin disease with a strong hormonal component, especially in women. Hormonal therapies are increasingly used in moderate-to-severe or treatment-resistant cases. This review aims to summarize current evidence on the efficacy and safety of hormonal treatments for acne.

Materials and Methods: A narrative review was conducted using PubMed, Scopus, and Web of Science, including studies published from 2010 to 2025. Eligible articles included randomized controlled trials, cohort studies, systematic reviews, and meta-analyses evaluating hormonal therapies such as combined oral contraceptives (COCs), spironolactone, cyproterone acetate, and topical antiandrogens (eg, clascoterone). Data were extracted on mechanisms of action, clinical efficacy, safety, and treatment indications to ensure consistent synthesis across therapies.

Results: Spironolactone consistently reduced lesion counts and improved quality of life in adult women, with good tolerability and a low risk of hyperkalemia. COCs effectively decreased both inflammatory and non-inflammatory lesions, with similar efficacy across different progestins. Clascoterone, a topical antiandrogen, showed significant improvement in lesion counts with minimal systemic absorption. Preliminary evidence also supports the use of topical spironolactone. Compared with antibiotics, hormonal therapies provide durable disease control and avoid antimicrobial resistance.

Conclusion: Hormonal therapies are effective and well-tolerated options for acne, particularly in women with hormonal patterns or refractory disease. By specifically targeting androgen-driven pathways, hormonal agents offer sustained improvement and should be incorporated into personalized acne management.

Keywords: acne vulgaris, hormonal therapy, treatment, management

Introduction

Acne vulgaris is a chronic inflammatory skin condition characterized by comedones, papules, pustules, nodules, and, in some cases, scarring lesions.[1] It is one of the most prevalent skin conditions globally, affecting approximately 9.4% of the population, making it the eighth most common disease worldwide.[2] Its onset typically coincides with puberty, but acne can persist or even begin in adulthood. Age-based classification includes adolescent acne, which generally appears between ages 12 and 18, and adult acne, which refers to cases developing after the age of 25.[3] A subset of adult acne, known as persistent acne, begins during adolescence and continues into adulthood, whereas late-onset acne arises de novo after the mid-twenties.[4] While adolescent acne shows a slightly higher prevalence in males, adult acne is more frequently observed in females and is often persistent or relapsing in nature.[1]

The pathogenesis of acne involves several interrelated mechanisms, including follicular hyperkeratinization, excessive sebum production, *Cutibacterium acnes* colonization, and inflammation. In females, hormonal imbalances, particularly involving androgens, can significantly contribute to the development and persistence of acne.[5] Clinical features such as premenstrual flares, resistance to conventional therapies, and the presence of acne in women with irregular menstrual cycles or signs of hyperandrogenism suggest a hormonal component.[6]

Received: 14 October 2025
Accepted: 2 December 2025
Published: 6 December 2025

Conventional acne therapies, including topical retinoids, benzoyl peroxide, systemic antibiotics, and oral isotretinoin, may be limited by tolerability issues, incomplete long-term control, risk of antimicrobial resistance, or strict safety and monitoring requirements.[1,7] Systemic antibiotics are effective but should be used for short durations due to rising resistance concerns, while isotretinoin, although highly effective, is associated with significant adverse effects and teratogenicity, which limit its use in many women of reproductive age.[1,7] In this context, multiple international guidelines recommend hormonal therapy as an evidence-based option for women with moderate-to-severe acne, adult or persistent acne, signs of androgen excess, or inadequate response to standard therapies.[1,7] Hormonal agents such as combined oral contraceptives and spironolactone are recognized as valuable alternatives or adjuncts, particularly in cases with a clear hormonal pattern.[1,7]

Given the central role of androgens in acne pathophysiology, hormonal therapies have emerged as a valuable option, especially in women with moderate-to-severe or recalcitrant acne.[7] These treatments include combined oral contraceptives (COCs), and antiandrogens such as spironolactone.[7] Hormonal treatments not only target the underlying endocrine drivers of acne but also offer long-term control with a favorable side-effect profile in appropriately selected patients.[8]

Due to the high burden of acne, the limitations of conventional therapies, and the need for more targeted approaches, it is essential to explore and understand the role of hormonal treatments in acne management. The objective of this review is to examine current evidence regarding the efficacy, safety, and clinical application of hormonal therapies in the treatment of acne.

Materials and Methods

This narrative review was conducted to synthesize the current literature on the role of hormonal therapies in the treatment of acne vulgaris. A comprehensive search of the electronic databases PubMed, Scopus, and Web of Science was performed to identify relevant articles published between January 2010 and June 2025. The following keywords and Boolean operators were used: "acne" AND "hormonal therapy" OR "antiandrogens" OR "oral contraceptives" OR "spironolactone" OR "androgens" OR "hyperandrogenism". Only articles published in English and involving human subjects were considered.

Eligible studies included randomized controlled trials (RCTs), meta-analyses, systematic reviews, cohort studies, and clinical guidelines that focused on the efficacy, safety, and clinical indications of hormonal treatments for acne. Articles were screened based on title and abstract, followed by full-text assessment. Studies primarily addressing topical treatments, non-hormonal systemic therapies, or acne pathogenesis without therapeutic focus were excluded.

The selected literature was analyzed to extract key findings on the mechanisms of action, indications, dosing, adverse effects, and clinical outcomes associated with hormonal agents, including combined oral contraceptives, spironolactone, cyproterone acetate, and other antiandrogens. Where available, data on treatment comparisons, long-term efficacy, and patient-reported outcomes were also considered.

Results

Topical Therapy: Clascoterone 1% Cream

Clascoterone is a novel first-in-class topical androgen receptor inhibitor approved by the FDA in 2020 for the treatment of acne vulgaris in patients aged 12 years and older. Unlike systemic anti-androgens, clascoterone acts locally on the skin without significant systemic absorption, making it a suitable alternative for both male and female patients who may not be candidates for hormonal or systemic therapy. It works by competitively inhibiting dihydrotestosterone (DHT) binding to androgen receptors in sebocytes and hair follicle cells, thereby decreasing sebogenesis and the downstream inflammatory cascade that contributes to acne pathogenesis.[9] A systematic review and meta-analysis of five randomized, placebo-controlled trials (n = 2457) demonstrated that twice-daily topical clascoterone significantly increases treatment success measured by Investigator's Global Assessment (IGA) (RR = 2.87; 95% CI: 2.11–3.89; $p < 0.001$), decreases non-inflammatory lesions with mean difference (MD) = −5.64; $p < 0.01$, and has no significant effect on inflammatory lesions (MD = −1.82; $p = 0.27$). Safety endpoints, including treatment-emergent adverse events (TEAEs), serious AEs, and discontinuations, did not differ from

placebo.[10] Pooled data from two Phase 3 RCTs involving 1440 patients aged 9–58 years found clascoterone superior to vehicle across all primary and secondary outcomes, with about 90% adherence and no systemic adverse effects noted. Local skin reactions were mild and similar in both groups.[11] A long-term open-label extension (up to 9 months) confirmed sustained efficacy: nearly 49% of facial and 52% of truncal acne patients reached IGA 0/1. TEAEs occurred in about 18%, with erythema and dryness being most common, and no new safety signals emerged.[12] A 2024 systematic review comparing clascoterone, trifarotene, and tazarotene across six RCTs (n = 5474) showed robust reductions in inflammatory lesion count (MD = −11.5), non-inflammatory lesion count (MD = −12.3), and treatment success (OR = 2.1), with no significant efficacy differences between agents, though tolerability profiles differed.[13] The study by Hebert et al (2023) pooled data from two Phase III trials involving 1421 patients aged ≥12 years with acne vulgaris treated with clascoterone 1% cream twice daily for 12 weeks. Treatment success (IGA score 0/1 with ≥2-point improvement) was achieved in 19.9% of clascoterone-treated patients versus 7.7% in the vehicle group ($p<0.0001$). Clascoterone led to significantly greater reductions in both inflammatory and non-inflammatory lesions. Clinical improvement was evident as early as week 2, and the treatment showed an excellent safety profile with only mild, local adverse events.[14] A long-term open-label extension trial (up to 9 months) confirmed the sustained efficacy of clascoterone, showing that 49% of patients with facial acne and 52% with truncal acne reached IGA 0/1 by study end. This extension study also showed minimal adverse effects, with only 18% of participants reporting TEAEs, most commonly skin irritation, which did not require discontinuation.[12]

Spironolactone

Spironolactone, an oral anti-androgen medication, has emerged as an effective off-label hormonal therapy for adult female acne.[15] It works by blocking androgen receptors and reducing sebum production, which helps decrease acne lesions. Spironolactone is generally well-tolerated, with side effects including menstrual irregularities and hyperkalemia.[16] Multiple RCTs and meta-analyses demonstrate its efficacy: a meta-analysis including seven RCTs (643 patients) found significant reductions in acne severity index (MD = –6.53; $p = 0.003$), with favorable safety profiles and no notable lesion count differences at early time points.[17] A dedicated systematic review and meta-analysis showed that spironolactone nearly doubles the odds of treatment success compared to placebo or doxycycline (pooled OR = 2.51) in moderate–severe acne among adult women.[18] Supporting evidence comes from the SAFA trial, a large double-blind RCT of 410 women over 24 weeks, which reported significant improvements in Acne-Specific Quality of Life and Investigator Global Assessment scores (OR = 5.18 at 12 weeks), with minimal side effects, mainly headache and lightheadedness.[19] At 12 weeks, patients receiving spironolactone showed modest but statistically significant improvements in acne-related quality of life, with Acne-QoL symptom subscale scores of 19.2 versus 17.8 in the placebo group (mean difference: 1.27).[19] More pronounced differences emerged at 24 weeks, where the spironolactone group scored 21.2 compared to 17.4 in the placebo arm (mean difference: 3.77).[19] In a pivotal 4-year retrospective cohort study, Grandhi & Alikhan evaluated spironolactone in 291.5 patient-years of treatment for post-adolescent acne, involving an unspecified number of adult female patients (totaling nearly 300 patient-years).[20] The study reported that 86% of patients experienced clinical improvement while on spironolactone therapy. Adverse events were notably infrequent and mild; importantly, hyperkalemia—a common concern with anti-androgens—remained rare and mostly clinically insignificant over the study period.[20] Common adverse effects include dizziness, headache, breast tenderness, and mild hypotension, all generally low-grade and dose related. Hyperkalemia in otherwise healthy young women is rare, suggesting routine potassium monitoring may be unnecessary in this population.[21] While animal studies prompted concerns over tumorigenesis, long-term human data have not shown carcinogenic risk.[21] In an eight-week pilot clinical trial, Ayatollahi et al evaluated the effectiveness and tolerability of a 5% spironolactone cream applied twice daily for mild to moderate facial acne in 15 patients. The study reported statistically significant reductions in inflammatory papules, open and closed comedones, and overall acne global grading at both 4 and 8 weeks compared to baseline.[22] No notable side effects occurred during treatment, and key skin parameters, such as hydration, erythema, transepidermal water loss (TEWL), pH, sebum levels, and *Propionibacterium acnes* activity, remained stable throughout the study.[22]

Combined Oral Contraceptives (COCs)

Clinical trials and meta-analyses consistently affirm that combined oral contraceptives, a combination of estrogen and progestin, are effective and well-tolerated treatments for moderate acne in women. Overall, these estrogen-progestin regimens work by suppressing ovarian androgen production and increasing sex hormone–binding globulin (SHBG), thereby reducing free testosterone and sebum production, while the inclusion of anti-androgenic progestins (eg, drospirenone, dienogest, cyproterone acetate) further enhances acne improvement.[23] A Cochrane review of 31 randomized trials (12,579 participants) demonstrated that COCs significantly decrease both inflammatory and non-inflammatory facial lesions compared to placebo. Levonorgestrel-COCs reduced total lesions by MD −9.98; drospirenone-COCs achieved OR 3.02 for clear skin.[24] In a randomized, double-blind study of drospirenone (3 mg)/ethinylestradiol (20 µg) taken in a 24/4 regimen, there was a four-fold higher chance of achieving "clear or almost clear" skin versus placebo after six cycles, with safety comparable to other low-dose COCs.[25] Analogously, a Phase III trial of EE 20 µg/drospirenone 3 mg in Chinese women reported a 66.8% reduction in total lesion count versus 37.7% with placebo and no unexpected adverse events.[26] Moreover, ethinylestradiol/dienogest (EE/DNG) COCs were shown to be superior to placebo and non-inferior to cyproterone acetate combos, reducing inflammatory lesions by 65.6% and total lesions by 54.7% after six months.[27] A real-world 12-month cohort using EE 20 µg/dienogest 2 mg demonstrated a dramatic 94% mean reduction in facial acne lesions, with nearly a quarter of women fully clearing.[28] A 2023 review of EE/norgestimate combinations reported over 50% reduction in inflammatory lesions (from 19.0 to 8.2 per patient), comedones (35.2 to 17.7), and total lesions (from 54.3 to 25.9) compared to placebo, with a favourable safety profile and low VTE risk.[29] Moreover, pooled analysis of two US trials involving EE 20 µg/drospirenone 3 mg (24/4 regimen) in nearly 900 women showed significantly greater reductions in inflammatory, non-inflammatory, and total lesions versus placebo ($P < 0.0001$), with an approximately threefold increase in the odds of achieving "clear or almost clear" skin.[30]

Discussion

The development of new systemic treatments for acne signals a shift toward therapies that target specific pathogenic mechanisms, prioritizing both safety and the preservation of antimicrobial efficacy. Despite these advances, isotretinoin continues to be the most potent systemic option, as demonstrated by network meta-analyses which consistently rank it highest for moderate-to-severe acne. At cumulative doses of 120 mg/kg or more, isotretinoin achieves an average lesion reduction of approximately 58% and demonstrates significantly higher odds of therapeutic success compared to placebo and alternative systemic agents.[31] Isotretinoin exerts wide-ranging effects by simultaneously reducing sebum secretion, normalizing follicular keratinization, dampening inflammation, and limiting *Cutibacterium acnes* proliferation. However, its strong efficacy is tempered by a notable side effect profile, including common mucocutaneous symptoms, potential lab abnormalities, mandatory teratogenic risk management, and rare but serious adverse events such as acne fulminans.[32] Hormonal treatments such as spironolactone and combined oral contraceptives (COCs) provide distinct advantages over conventional topical and systemic therapies, particularly by targeting the androgen-mediated pathogenesis of acne in women. It should be noted that the evidence base is not evenly distributed across hormonal therapies; spironolactone and COCs remain the most extensively studied agents, whereas data for topical antiandrogens and cyproterone acetate are comparatively limited. This disparity likely reflects the current research landscape rather than a true difference in clinical relevance. Although there are no comparative studies between isotretinoin and systemic hormone therapies against acne, Faghihi et al evaluated the efficacy of cyproterone acetate (CPA) and isotretinoin (0.75 mg/kg/day) over four months in 30 women diagnosed with SAHA syndrome, a condition marked by seborrhea, acne, hirsutism, and alopecia due to androgen excess. Both treatment groups showed statistically significant reductions in the ASI. However, isotretinoin was not superior to CPA, indicating that hormonal modulation can be as effective as retinoid therapy in androgen-driven acne phenotypes. Additionally, CPA showed a better profile in treating other androgen-related symptoms like hirsutism and alopecia, suggesting its advantage in multi-symptom management within this patient group.[33] In a randomized trial involving 133 women with moderate acne, spironolactone plus benzoyl peroxide was significantly more effective than doxycycline plus benzoyl peroxide at 4 and 6 months ($p = 0.007$), demonstrating superior lesion reduction and quality-of-life improvements, with good tolerability in the spironolactone group.[34] Meta-analyses further support spironolactone's

efficacy, showing that oral spironolactone nearly doubles the odds of treatment success compared to placebo or doxycycline (OR = 2.51) and produces clinically meaningful reductions in acne severity index (MD = –6.53; p = 0.003).[34] The SAFA trial, a large RCT with 410 women, confirmed significant improvements in acne severity with the use of spironolactone and patient-reported outcomes at 12 and 24 weeks, with primary side effects limited to mild headache and dizziness. These findings suggest that spironolactone not only rivals but may surpass antibiotic-based regimens in long-term management, while mitigating concerns of antibiotic resistance.[35] Moreover, the efficacy outcomes of the study by Kultun et al on the drospirenone/EE association are comparable to systemic antibiotics by six months but with the advantage of reduced risk of antibiotic resistance.[25] Another head-to-head RCT comparing COCs containing drospirenone versus chlormadinone acetate over nine cycles showed similar median lesion count reduction (62% vs 59%) and comparable suppression of sebum production and androgen levels.[36] This confirms that different progestins in COCs offer broadly equal acne control.

Regarding topical therapies, conventional topical treatments like benzoyl peroxide and retinoids provide local antimicrobial and anti-inflammatory effects but lack systemic hormonal modulation. While topical clascoterone shows promise in reducing sebum production, hormonal therapies uniquely address hyperandrogenism, thus providing sustained improvement particularly in hormonally driven, refractory adult acne.[37] In a clinical study involving 38 participants, applying a 5% spironolactone gel twice daily led to a 71% decrease in total lesion count, compared to a 36% reduction observed with the placebo gel (vehicle).[38] In a 12-week clinical trial involving 35 male and female patients with mild-to-moderate acne, twice-daily application of a 2% topical spironolactone solution resulted in a greater average decrease in comedones (4.6), papules (3.8), and pustules (1.9) compared to once-daily use of a 1.5% topical clindamycin solution.[39]

Regarding safety, spironolactone is generally well tolerated in the treatment of acne among otherwise healthy women, with side effects such as menstrual irregularities, mild hypotension, headache, and dizziness being uncommon and typically low-grade, while clinically significant hyperkalemia is rare, occurring at a rate (approximately 0.7%) equivalent to baseline levels in this population, indicating that routine potassium monitoring is often unnecessary unless additional risk factors are present.[40] COCs carry a modestly elevated risk of arterial and venous thrombotic events, approximately two- to threefold higher compared to non-users. This increase remains small in absolute terms, and an extensive body of evidence confirms that, in the absence of contraindications and when appropriate risk factors such as smoking or hypertension are excluded, COCs continue to maintain a favorable safety profile, with serious events being rare and the overall benefit-to-risk ratio remaining positive for acne treatment and contraception purposes.[41]

Conclusions

Hormonal therapies, including combined oral contraceptives and spironolactone, are effective and well-tolerated options for managing moderate to severe acne, especially in women with hormonal imbalances. These treatments target androgen-driven pathways, providing sustained improvement and addressing related symptoms. Topical antiandrogens like clascoterone and spironolactone offer promising alternatives with fewer systemic effects. Compared to antibiotics, hormonal therapies may offer equal or superior efficacy while reducing risks of resistance. Although isotretinoin remains the most potent systemic therapy, hormonal treatments are valuable for specific patient populations and can be safely incorporated with proper monitoring.

However, each therapy has specific adverse effects: combined oral contraceptives carry a small but increased thromboembolic risk; spironolactone may cause menstrual irregularities, breast tenderness, and mild hypotension, while hyperkalemia is uncommon in healthy women; topical antiandrogens are mainly associated with mild local irritation. Recognizing these safety profiles helps tailor therapy to individual risk factors.

Overall, hormonal approaches should be considered integral in personalized acne management to improve long-term outcomes.

Data Sharing Statement

Data that support the findings of this study are available from the corresponding author, upon reasonable request.

Funding

There is no funding to report.

Disclosure

None of the contributing authors has any conflict of interest, including specific financial interests of relationships and affiliation relevant to the subject matter or discussed materials in the paper.

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