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Review Article

Role of Anti-Androgens in the Management of Polycystic Ovary Syndrome (PCOS)

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common hormonal disorder in women of reproductive age. It is marked by high levels of androgens, problems with ovulation, and the presence of many cysts in the ovaries. Anti-androgens (AAs), such as spironolactone, flutamide, finasteride, and cyproterone acetate (when taken with ethinyl estradiol), are often used to manage symptoms caused by excessive androgens, mainly hirsutism and acne. They may also help with other metabolic or adnexal issues. This review covers the mechanisms behind these treatments, their clinical effectiveness, evidence comparing them, safety concerns (especially liver damage and risks to a developing fetus), recommendations from guidelines, and practical prescribing tips. Key evidence supports the use of anti-androgens, typically with effective contraception, for managing symptoms of high androgen levels when pregnancy is not intended. However, there are still uncertainties regarding long-term safety, effects on metabolism, and direct comparisons among different agents. Future research on anti-androgens in PCOS aims to improve metabolic health, lower long-term risks related to heart and metabolism, and increase ovulation rates in women with high androgen levels. Studies are looking into combination treatments for severe hair loss, safe use in adolescents, personalized approaches based on genetic profiles, and new topical forms to lower systemic risks. Long-term management for stubborn hirsutism also remains a major focus.

INTRODUCTION

PCOS affects up to 8–13% of reproductive-age women depending on diagnostic criteria and population studied and frequently presents with clinical or biochemical hyperandrogenism. Excess androgens drive hirsutism, acne, androgenic alopecia, and contribute to psychosocial morbidity. First-line management emphasizes lifestyle modification and, for many patients, combined oral contraceptives (COCs) to suppress ovarian androgen production; however, anti-androgens are often added or used when COCs

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alone are inadequate or contraindicated. Recent international and specialty guidelines outline roles for anti-androgens primarily in symptomatic care of hyperandrogenism.

Mechanisms of Action

Anti-androgens used in PCOS act through several mechanisms:

Androgen receptor antagonism — Spironolactone and flutamide directly block androgen receptors, reducing target tissue androgen effects (hirsutism, acne).

5α-reductase inhibition — Finasteride inhibits conversion of testosterone to dihydrotestosterone (DHT), reducing DHT-mediated hair follicle stimulation.

Progestogenic antiandrogenic effects — Cyproterone acetate (CPA) is a progestin with strong anti-androgenic activity and is used as part of a combined oral contraceptive (CPA/EE).

Pharmacologic differences influence onset of clinical effect (typically months for meaningful improvement in hirsutism), relative contraindications (e.g., pregnancy), and side-effect profiles.

Individual Agents — Evidence Summary

Spironolactone

Use & dosing: Typical oral doses 50–200 mg/day for hirsutism/acne; commonly used together with COC for contraception in women not seeking pregnancy.

Efficacy: Multiple trials and meta-analyses show spironolactone reduces Ferriman-Gallwey scores and acne severity compared with placebo or baseline; similar efficacy to other anti-androgens when studied head-to-head.

Safety: Side effects include menstrual irregularities (when not on COC), hyperkalemia (rare in young healthy women without renal disease), fatigue, and breast tenderness. Spironolactone is teratogenic risk for feminization of male fetus — must be used with reliable contraception.

Flutamide

Use & dosing: Non-steroidal androgen receptor antagonist; low doses (62.5–250 mg/day in many studies) used for hirsutism and metabolic outcomes in PCOS trials.

Efficacy: RCTs and meta-analyses show flutamide reduces hirsutism scores and may have beneficial effects on body fat distribution and insulin sensitivity in some trials.

Safety: Hepatotoxicity is a major concern (cases of severe liver injury reported), which limits widespread use; regular liver function monitoring is recommended if used. Teratogenic risk mandates contraception.

Finasteride

Use & dosing: 5α-reductase inhibitor, trial doses vary (1–5 mg/day). Often considered for androgenic alopecia or hirsutism when other agents not suitable.

Efficacy: RCTs and systematic reviews support some benefit for hirsutism/hair loss, though effect size is modest and slower to appear compared to receptor antagonists.

Safety: Generally well tolerated; teratogenic risk (male fetal external genitalia abnormalities) —

strict contraception required for women of childbearing potential.

Cyproterone Acetate (CPA) (as part of CPA/EE combined pill)

Use & dosing: CPA combined with ethinyl estradiol (EE) is used widely in some regions for acne and hirsutism.

Efficacy: Trials and reviews show CPA/EE reduces hirsutism and biochemical hyperandrogenism and may be more effective for hirsutism than some other COCs.

Safety: Risks include thromboembolism (class risk with combined estrogen-containing contraceptives) and, with higher CPA exposure, concerns about mood effects and liver function monitoring in some cases. CPA is not available or is restricted in some countries.

Comparative Effectiveness

Systematic reviews and meta-analyses suggest that anti-androgen therapies (alone or combined with COCs) are generally superior to placebo or non-antiandrogen approaches for reducing hirsutism and acne scores. Direct comparisons among spironolactone, flutamide, and finasteride show broadly similar efficacy, though adverse effect profiles differ (flutamide: hepatotoxicity; spironolactone: menstrual changes and potassium effects; finasteride: teratogenicity concerns and variable efficacy). A 2023 meta-analysis concluded that anti-androgens plus lifestyle were superior to metformin plus lifestyle for hirsutism reduction.

Safety Considerations & Monitoring

Teratogenicity: All oral anti-androgens carry teratogenic risk (feminization/ambiguous genitalia or external genital effects in male fetuses). Anti-androgens must never be given to pregnant women, and reliable contraception is mandatory during treatment and for a washout period as recommended per agent.

Hepatotoxicity: Flutamide has been associated with severe liver injury; baseline and periodic liver function tests (LFTs) are advised if flutamide is chosen.

Metabolic effects: Evidence for beneficial metabolic effects of anti-androgens is mixed; some studies suggest favorable changes in fat distribution but consistent long-term metabolic benefit is unproven. Monitoring lipids and glucose per PCOS guidance remains important. Other adverse effects: Spironolactone — hyperkalemia in predisposed patients; CPA/EE — thromboembolic risk; finasteride — possible mood changes or sexual side effects reported in some series. Regular counselling and targeted lab monitoring are recommended.

Guideline Recommendations and Practical Approach

When fertility is desired: Anti-androgens are not used for conception; instead, focus on lifestyle, ovulation induction strategies (letrozole), and metabolic care.

When fertility is not desired and hyperandrogenic symptoms are bothersome: First-line options often include COCs; add or substitute anti-androgens when COCs alone are insufficient or contraindicated. Use of spironolactone is common due to a favorable balance of efficacy and tolerability; flutamide may be effective but is limited by hepatotoxicity; finasteride can be considered for hair loss. CPA/EE is effective but carries estrogen-related risks.

Combination therapy: Many clinicians combine COCs with an anti-androgen (e.g., spironolactone) to both suppress ovarian androgen production and block peripheral androgen action; this reduces teratogenic risk but contraception must be reliable.

Gaps in Evidence and Research Priorities

1. Long-term safety: Longitudinal data on metabolic, cardiovascular, and hepatic outcomes over many years are limited.
2. Head-to-head RCTs: Comparative trials directly comparing spironolactone vs flutamide vs finasteride on both efficacy and safety endpoints are sparse.
3. Effect on metabolic endpoints: Clear, reproducible evidence that anti-androgens improve insulin resistance or reduce long-term cardiometabolic risk is lacking.
4. Regional/agent availability and regulatory differences: CPA availability and safety profiles vary globally; policy and product availability affect practice.

Practical Prescribing Checklist

Confirm diagnosis of PCOS and rule out alternative causes of hyperandrogenism.

Counsel on expected timelines (≥3–6 months for noticeable hirsutism improvement; up to 12 months for maximal effect).

If using anti-androgens in women of childbearing potential:

Use combined contraception or another reliable method concurrently.

Baseline and periodic LFTs if using flutamide; consider baseline electrolytes/renal function with spironolactone.

Inform patients about common side effects and when to seek care.

Reassess every 3 months for efficacy and adverse effect monitoring; consider dose adjustments or switching agent if poor response or intolerance.

Future Indications & Studies — Anti-androgens in PCOS

1. Adjuvant therapy to improve metabolic phenotype (insulin resistance / visceral adiposity)

Rationale: androgens influence adipose tissue distribution; small trials suggest possible beneficial effects on fat distribution and insulin sensitivity. Investigate whether anti-androgens (esp. spironolactone or flutamide alternatives with safer hepatic profiles) improve metabolic endpoints when combined with lifestyle or insulin-sensitizers.

2. Prevention of androgen-related cardiometabolic risk in high-risk PCOS

Rationale: long-term cardiovascular risk in PCOS is increased; test whether anti-androgen therapy started in young adulthood reduces intermediate cardiovascular risk markers (vascular stiffness, carotid intima media thickness, inflammatory markers).

3. Adjunct to ovulation induction in hyperandrogenic, anovulatory PCOS (non-pregnancy intent phase)

Rationale: temporarily reducing peripheral androgen action prior to ovulation induction with letrozole or gonadotropins might improve follicular response or reduce miscarriage (exploratory).

4. Management of severe androgenic alopecia in PCOS with combination systemic and topical therapy

Rationale: combine finasteride or spironolactone with topical minoxidil or new topical anti-androgens to maximize hair preservation with minimized systemic exposure.

5. Treatment of adolescent PCOS with predominant cutaneous androgen symptoms

Rationale: carefully evaluated low-dose regimens for adolescents (after growth completed) could address early psychosocial morbidity; safety and long-term effects need dedicated study.

CONCLUSION

Anti-androgens are valuable agents in the symptomatic management of hyperandrogenism in PCOS, particularly for hirsutism and acne in women not pursuing pregnancy. Spironolactone is widely used due to demonstrated efficacy and tolerability; flutamide and finasteride have roles in selected patients but are limited by safety concerns and teratogenic risk. International guidelines recommend anti-androgens as part of a multimodal approach (lifestyle, COCs when appropriate) for symptom control. Treatment selection should be individualized based on symptom severity, comorbidities, pregnancy plans, and drug safety profiles. Further high-quality trials and long-term safety studies are needed to refine agent choice and dosing.

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CONFLICT OF INTEREST

All of the authors affirm no conflicts of interest.

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