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Updates to Acne Vulgaris Treatment: A Review of a Topical Androgen Receptor Inhibitor

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Updates to Acne Vulgaris Treatment: A Review of a Topical Androgen Receptor Inhibitor

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Abstract

Acne Vulgaris is an inflammatory skin disorder that is common among adolescents and young adults. Acne is defined as a chronic inflammatory dermatosis which consists of open comedones (blackheads), closed comedones (whiteheads) and inflammatory lesions.¹ There are many ways to combat acne, one of which is to stop the effects of androgens on androgen receptors. Here we will review Clascoterone, a medication approved for the treatment of acne. Clascoterone is the first topical medication to target the hormonal pathogenesis of acne. It was approved by the FDA in 2020 and is effective in treatment of acne vulgaris in patients 12 years of age and older.²

Pathophysiology & Past Treatments

- The etiology of acne vulgaris is multifactorial and includes:
 - genetic predisposition, hormonal factors, follicular hyperkeratosis, and colonization with *Cutibacterium acnes*³
- Androgen hormones stimulate the increased production of sebum and are therefore an important target for treatment⁴
- Previously, the only way to target acne caused by androgenic effects on androgen receptors were through systemic medications
 - this was primarily accomplished with oral contraceptives and spironolactone⁵
- As with most systemic drugs these medications have a wide side effect profile
 - Oral contraceptives can cause a serious side effect of thrombosis.⁶
 - Spironolactone can lead to menstrual irregularities, increased urination, headaches, dizziness, nausea, and vomiting.⁷

Discussion

- Acne vulgaris is an inflammatory disorder that can be highly distressing for patients
- The exact etiology is multifold, which allows for a wide range of potential targets
- There are many existing treatments available on the market for the treatment of acne
- Nearly all of the drugs that target the effects of androgen hormones on androgen receptors are systemic drugs
- Clascoterone is the only topical antiandrogen approved by the FDA
- Clascoterone works to block the androgen receptor so that androgens can't bind to it
- Clascoterone's low side effect profile makes it a viable treatment option for patients that can't tolerate the side effects of systemic antiandrogens
- This review demonstrates the importance of Clascoterone in the treatment of acne and that future efforts should be made to develop more topical drugs that can act as androgenic inhibitors
- Further studies are needed on the long-term safety of Clascoterone and its efficacy in combination with other acne medications ²

Abstract

- Acne is an inflammatory skin disease that is found in about 80% of adolescents and young adults.¹
- It is more common in girls in the age range of 12 and younger but it presents more in boys in the age range of 15 and older.¹
- Acne usually resolves by twenty years of age; however, it can persist into early adulthood, especially in females ¹
- Acne has many negative effects like emotional distress, low self esteem, anxiety, and can even lead to permanent skin damage ^{1,2}
- Past research suggests that genetics combined with hormones (especially androgens) lead to the production of excess sebum which contributes to acne lesions.^{1,2}
- Acne has been treated topically (Retinoids, Antibiotics etc.) or systemically (Isotretinoin, Antibiotics, Spironolactone etc.) ^{1,2}
- Clascoterone is the only currently FDA approved topical androgen antagonist.

Pathophysiology & Past Treatments

- Cortexolone 17 α -propionate or Clascoterone is an androgen receptor antagonist that actively competes with dihydrotestosterone⁸, an androgen, from binding to the androgen receptor
- The androgen receptor is a member of the hormone nuclear receptors that has three functional domains⁹
 - ligand binding domain
 - N-terminal transcriptional regulation domain
 - DNA binding domain
- When these domains are acted on they can carry out several downstream effects that lead to formation of acne
- Clascoterone blocks the downstream effects of dihydrotestosterone by competing for the androgen receptor
- Dihydrotestosterone is prevented from enacting androgen receptors that lead to sebaceous gland proliferation, excess sebum production, and inflammation.¹⁰
- Clascoterone has the benefit of not being a systemic drug, making its side effect profile not as severe as the systemic medications previously used to treat acne:
 - telangiectasia, skin atrophy, striae rubrae, erythema, edema, scaling/dryness, stinging/burning, and pruritus.¹⁰

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