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Review Article

A review article on Winlevi

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ABSTRACT

Acne is a most common multiform skin condition. Androgen plays a major role in acne pathogenesis in both males and females. The appliance of anti-androgen is potentially effective. However, anti-androgens for topical application are not available in market. Clascoterone (cortexolone 17α propionate), an ester derivative of cortexolone is an androgen receptor inhibitor developed as a topical cream and solution for the treatment of androgen dependent skin disorders, including acne vulgaris. Although the mechanism of action of clascoterone (Winlevi) for topical treatment of acne vulgaris is not known. In 2020 clascoterone 1% has been first approved by United States of America (USA) for the topical therapy of acne vulgaris people aged 12 years or above. Assessment of acne is done based on overall severity of acne based on grades- grade 0, grade 1, grade 2, grade 3, and grade 4 (clear- severe). Both inflammatory on non-inflammatory lesions were counted. Treatment success is achieved when the grade or score is clear or almost clear. Clascoterone cream is well tolerated with no significant clinical safety issues. Clascoterone 1% twice daily treatment have the most effective favourable results with low adverse events. Currently first line treatment targeting aspects of acne includes benzyl peroxide topical or oral antibiotics, topical retinoid. Females with acne is treated with combined oral contraceptives (e. g. norgestimate and norethindrone are approved by FDA for treatment of acne in females) or spironolactone which affects androgens. Androgen receptors are present throughout the skin and found in sebaceous glands, dermal cells, and sebocytes. Androgen inhibiton is an effective way for treatment of acne in females.

Keywords: Acne, Clascotrone, Inhibition, Treatment, Phases

INTRODUCTION

Acne is the eight most common conditions in the world; it is a sustained disorder of pilosebaceous in which genetic predisposition, bacterial infection, endocrine factors follicular hyperkeratinisation adds to its onset and persistence.[1,2] It is common in young adults of age 12-25 years and 85% of pubescent.[1]

Acne vulgaris is a common inflammatory skin condition which is characterized by raised sebum production, inflammation and colonization with cuti bacterium acnes.[13] Approaches in perception of pathogenesis of androgen related conditions have forced to the development of treatment targeting the synthesis of androgens or their binding to androgen-receptor.[2] Currently first line therapy addressing acne pathophysiology includes topical retinoid, benzyl peroxide, topical antibiotics and oral antibiotics.[1]

Clacoterone (Winlevi) is an androgen receptor inhibitor which is being advanced as a topical cream and solution for therapy of androgen dependent dermal disorders.[2] The exact mechanism of action is unknown.[2] The drug is considered to compete with androgen dihydrotestosterone to bind to androgen receptors in sebaceous gland to attend necessary pathogenesis for acne vulgaris.[1] Topical clascoterone 1% cream is a new chemical entity used in the treatment of acne in both genders.[1] The steroid can easily penetrates into skin and metabolize quickly and

effectively into free indolent cortexolone.[12] It is suggested after cleaning the affected area clascoterone is being applied in a thin uniform layer two times daily in morning and evening.[2]

Figure 1: Winlevi ointment.[14]

PHARMACOKINETICS

Absorption

Topical application of Winlevi 1% of mean dose of 6 g approximately for 2 weeks twice daily in adults with moderate to severe vulgaris reached steady state systemic concentration by day 5.[2,10]

Distribution

In *in vitro* plasma protein binding is 84-89% and is not dependent on concentration.[2,10]

Metabolism

In patients aged greater than or equal to 12 years of age having acne vulgaris on treatment with Winlevi cream, plasma concentration of cortexolone a primary metabolite of clascoterone were detectable and in general below or near the lower limit of quantitation of 0.5 ng/ml.[2,10]

Excretion

It is not fully characterised in humans.[2,10] Winlevi has no clinical effects on pharmacokinetics of drugs metabolised by CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4.[2,10]

PHARMACODYNAMICS

Cortexolone 17α-propinoate is an ester derivate of cortexolone. It is potent anti-androgen with selective topical activity. When compare to other anti-androgens topical clascoterone is four times more potent than progesterone, three times more potent than flutamide, approx. two times more potent than finasteride. Winlevi cream 1% on systemic exposure with maximum dose did not prolong QT-interval. Potassium levels has been elevated in 5% of clascoterone treated patients when compared with 4% of vehicle treated patients.[2,10]

MECHANISM

The mechanism of action is unknown, but in in vitro studies it shows that clascoterone binds to androgen receptors with high affinity and inhibits DHT stimulated signalling. It doses dependently inhibits DHT induced lipid synthesis and inflammatory cytokine production in human sebocyts.[2,10]

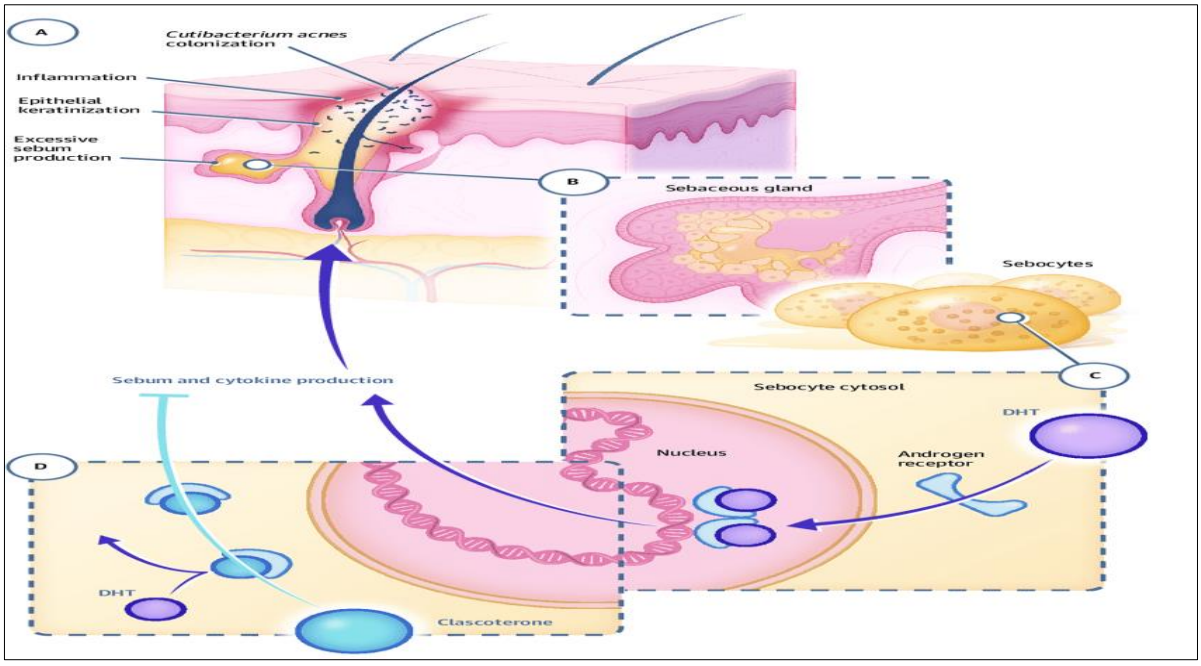

Figure 2: Mechanism of action.[15]

TREATMENT

Winlevi 1% applied daily twice for 12 weeks is more effective in reducing acne lesions in patients and achieving treatment success.[2] The product is self-applied in adequate quantity only to the affected area of face at bed time.[12]

Figure 3: Results before and after treatment.[16]

ASSESSMENT

The following four parameters were assessed at the screening and at the end of the weeks 2, 4, 6, and 8. The severity of acne was assessed based on each type of lesion: 0-comedones, 1-papules, 2-pustules, and 3-nodules. The multiplying each type of lesion severity score was obtained. Assessment was made on an ordinary scale with five severity scales" grade 0- clear skin with or without inflammatory lesions; grade 1- almost clear skin with rare non inflammatory lesions and not more than one small inflammatory lesion; grade 2- mild severity >grade 1 with not more than few inflammatory lesions and some non-inflammatory lesions; grade 3- moderate severity >grade 2 many non-inflammatory lesions and some inflammatory lesions but not more than one small nodular lesion; and grade 4- severe >grade 3 many inflammatory and non-inflammatory lesions not more than few nodular lesions.[12]

CONCLUSION

Clacscoterone 1% is first line agent for acne treatment which is a potent alternative to antibiotics and show promising results.

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