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Excimer Light and Topical Adapalene/Benzoyl Peroxide Gel in Treatment of Acne Vulgaris

Alaa Mohamed Kotp Nofal[1]*, Esraa Elsayed Elhawary[1], Dalia Salah Ashour[2], Amany Mohammad Abdel-Latif[1]

Departments of [1]Dermatology and Venereology and [2]Parasitology, Faculty of Medicine, Tanta University, Egypt

*** Corresponding author:** Alaa Mohamed Kotp Nofal**, Mobile:** (+20) 01069401105, **Email:** LoloMoaz160@gmail.com

ABSTRACT

Background: Acne vulgaris (AV) is a common chronic inflammatory dermatological illness that substantially affects quality of life, especially in adolescents and young adults. The primary topical retinoid utilized in the management of mild to moderate AV involves Adapalene (ADP). Benzoyl Peroxide (BPO) generates free oxygen, facilitating the breakdown of bacterial proteins and demonstrating bactericidal efficacy against P. acnes. The combined ADP 0.1%/BPO 2.5% gel was offered as a management for AV. It integrates anti-inflammatory, comedolytic, keratolytic, and antibacterial characteristics. Excimer light refers to a type of ultraviolet (UV) light produced by an excimer laser, which is a type of gas laser and induces apoptosis in keratinocytes and T lymphocytes.

Objective: This study aimed to highlight the role of Excimer Light and Topical Adapalene/ BPO Gel in Treatment of AV. **Methods:** We searched Science Direct, Google Scholar, and PubMed for Excimer Light, Adapalene, Benzoyl Peroxide and Acne Vulgaris. All were searched through the period from May 2011 to May 2024. The writers also reviewed relevant literature references, although they only included the most recent or comprehensive study. Documents in languages other than English have been excluded due to lack of translation sources. Unpublished papers, oral presentations, conference abstracts, dissertations, and other works that were outside the scope of large-scale scientific studies were excluded.

Conclusion: Combined excimer light and ADP/BPO or ADP/BPO alone could be utilised as effective therapy for AV.

Keywords: Excimer light, Adapalene, Benzoyl peroxide, Acne vulgaris.

INTRODUCTION

Acne vulgaris is among the most prevalent dermatological conditions encountered in practice, and it has been estimated that as many as 85% of people suffer from acne throughout their lives. While acne often begins at puberty and affects adolescents, it is increasingly reported to persist into later decades of life [1].

Acne therapy is contingent upon the kind, severity, anatomical location, and personal desire. The first treatment for mild AV is the topical use of retinoids, benzoyl peroxide (BPO), or a combination thereof. Adapalene is a synthetic third-generation retinoid accessible in cream, gel, and lotion formulations, where it is present in a suspension of lipophilic microcrystals of 3 to 10 µm in diameter [2].

This size of particles enables adapalene to selectively infiltrate pilosebaceous canals, the targeted location in AV. BPO is often employed with clindamycin, erythromycin, or adapalene to inhibit and, when taken with antibiotics, to avert the development of antibiotic-resistant strains of Cutibacterium acnes [2].

Excimer light is a kind of NB-UVB which produces a wavelength of 308 nm and offers tailored phototherapy treatments. The absorption of 308 nm light by dermal cells induces therapeutic effects in numerous prevalent and UV-responsive dermatological conditions [3].

ACNE VULGARIS

AV is a persistent inflammatory condition of the pilosebaceous unit that undergoes a chronic course. This prevalent dermatological condition is marked by the repeated emergence of pustules, papules, or nodules on the neck, trunk, face, or proximal upper limbs [4].

AV is prevalent and mostly affects teenagers and young adults. The predicted incidence of AV among teenagers varies from 35% to over 90% [5]. AV is among the most prevalent chronic dermatological conditions in the United States, impacting about 50 million individuals annually, mostly teens and young adults [6]. Prior Egyptian research indicated a self-reported acne prevalence of 34.7%. Females observed acne more commonly than males, with rates of 39.1% compared to 30.3% ($p = 0.009$) [7].

Acne frequently starts during the pre-adolescent phase (ages 7 to 12 years) and resolves by the 3rd decade, but it may continue into adulthood or emerge again in adulthood. Adolescent AV shows a male preponderance, but post-adolescent acne mainly impacts females [8, 9].

First-line treatments involve topical retinoids, azelaic acid, BPO, or combinations of these topical substances. For more severe conditions, oral antibiotics like doxycycline or minocycline, hormonal treatments that include combination of oral contraceptives or isotretinoin or spironolactone are the most efficacious [10].

Topical retinoids

Topical retinoids are compounds of vitamin A, Its interaction with their receptors (retinoic x and acid

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receptors) in keratinocytes diminishes follicular hyper-keratinization and lowers adhesions [11].

This impact not only inhibits comedogenesis but may also improve the absorption of other topical acne treatments. Moreover, retinoids possess anti-inflammatory properties via blocking the transcription factor AP1 activation and downregulating the expression of TLR2 [12].

Topical antibiotics

Clindamycin and erythromycin are the predominant topical antibiotics utilized for acne therapy, each available in various formulations. Antibiotics, whether oral or topical, aren't designed to serve as a standalone treatment for acne. Topical antibiotics ought to be utilized only in conjunction with BPO or topical retinoids to avert the emergence of antibiotic-resistant microorganisms [13].

Oral antibiotics

Doxycycline and minocycline have supplanted erythromycin and tetracycline in the majority of acne treatment cases. Doxycycline, tetracycline, and minocycline are contraindicated during pregnancy and in children under nine years of age; erythromycin is the only suggested alternative in these situations. Azithromycin is rarely utilized because of the potential for heightened resistance, a significant concern in other disorders. Tetracyclines manage acne via their direct anti-inflammatory impacts with their antibiotic properties. Hence, utilizing subantimicrobial dosages of doxycycline shows promise, however more research is required in this area. While, minocycline is beneficial for acne therapy, its advantage over other tetracyclines remains unproven [14].

Hormonal therapy

Hormonal therapies may be used with other AV treatments for postmenarcheal to premenopausal females with moderate-to-severe AV who don't plan to conceive. This medicine will also enhance the condition of mild acne in people using it for menstrual cycle abnormalities, contraception, or those experiencing cyclical acne exacerbations. Hormonal treatment may be inadequately utilized for women with acne [15]. Evaluation of hormonal treatment outcomes requires a duration of 6 to 12 months [16].

ADAPALENE

Adapalene (ADP) is a retinoid sanctioned by the U.S. Food and Drug Administration (FDA) for AV therapy, exhibiting less adverse effects compared to tretinoin [17].

Mechanism of Action

Retinoids action mechanism relies on their unique interaction to receptors of retinoid. Retinoids that target RARs influence cellular differentiation and proliferation [18]. This group includes adapalene, tretinoin, and tazarotene, which can be safely utilized in the management of psoriasis, AV, and photoaging [18].

Adapalene preferentially interacts with RARs but cannot form associations with cytosolic retinoic acid binding proteins, hence activating genes that govern cell development. Adapalene has a strong affinity for RAR-γ receptors located in the epidermis and for RAR-β receptors mostly found in dermal fibroblasts; however, it isn't as selective a RAR-γ agonist as trifarotene [19].

Consequently, the particular binding of RARs (RAR-γ and RAR-β) results in ADP inhibiting cell growth in a manner similar to tretinoin. While, the action mechanism remains incompletely elucidated, topically administered adapalene regulates inflammation, keratinization, and the differentiation of follicular epithelial cells. The development of microcomedones and inflammatory lesions linked to AV is diminished [19].

A research on hamster sebocytes has shown the inhibitory effect of adapalene on accumulation of sebum. This function pertains to the transcriptional repression of diacylglycerol acyltransferase 1, an enzyme involved in triacylglycerol production, and perilipin 1, a protein associated with lipid droplets. Furthermore, adapalene inhibits the development of sebum storage droplets in differentiated sebocytes induced by insulin, 5α-dihydrotestosterone (5α-DHT), and peroxisome proliferator-activated receptors (PPARγ) [20].

BENZOYL PEROXIDE

BPO is an over-the-counter topical medication and an FDA-sanctioned prescription therapy for AV. It has antibacterial effects against Cutibacterium acnes on the skin and within hair follicles [21].

Mechanism of Action

BPO has bactericidal properties towards Cutibacterium acnes, a key factor in AV. BPO, upon absorption by the skin, is transformed into benzoic acid BA. About 5 percent of BA is absorbed systemically and eliminated via the kidneys [22].

The residual BA is processed by cysteine in the dermis, emitting reactive oxygen species that lead to the oxidation of bacterial proteins. AV improvements is achieved by the diminution of free fatty acids (FFA), lipids, and P. acnes [23].

Following the daily application of 10% BPO for 2 weeks, the quantity of P. acnes in follicles of hair diminished by 98%, while the level of FFA fell by 50%, equal to outcomes seen following 4 weeks of treatment with antibiotics [24].

BPO used topically has modest sebostatic action, enhancing its keratolytic activities and efficiency in managing comedonal acne. BPO addresses cutaneous ulcers by promoting the healthy formation of granulation tissues and facilitating fast epithelial ingrowth [25].

BPO monotherapy enhances inflammatory acne, with mechanisms of action including antibacterial,

keratolytic, anti-inflammatory properties, and wound-healing capabilities [26].

BPO gel, although more effective compared to any prescription antibiotics towards P. acnes, is suitable for human usage. Low-strength (2.5% or 5%) BPO is advised, since it is less irritating and as efficient as higher concentration formulations [26].

In the case of BPO, similar to adapalene, the duration required to get a 25% decrease in the average count of inflammatory lesions remains consistent across various frequencies in individuals with mild-to-moderate papulopustular AV. Nonetheless, BPO seems to have a more rapid effect than topical tretinoin, adapalene, and isotretinoin [27].

Reports indicate that therapy with BPO alone is effective for mild inflammatory acne, due to the expense of retinoids, safety considerations, and favorable outcomes. BPO is additionally offered as a fixed-dose combination medication with adapalene, which helps simplify treatment regimens [28].

COMBINATION

Adapalene improves the absorption of BPO via modifying the follicular microenvironment. Consequently, from a theoretical perspective, the fixed combination of BPO and adapalene ought to demonstrate more efficacy than the individual drugs. Adapalene/BPO gel is both safe and extremely efficient for the management of AV. Its effectiveness, tolerability, and ease of utilization surpass those of other topical AV treatments, and its application doesn't promote antibiotic resistance [29].

The combined ADP 0.1%/BPO 2.5% gel is being offered as a treatment for AV. It integrates anti-inflammatory, comedolytic, keratolytic, and antibacterial characteristics [30]. ADP/BPO (0.3%/2.5%) is recommended for individuals aged 12 years and older [2].

ADP/BPO demonstrated superior efficacy compared to adapalene, with a decrease in inflammatory lesions ranging from 46% to 57.1%, supported by Level 1 evidence. In BPO, the decrease in inflammatory lesions varied between 44% and 71.8%. This outcome was equivalent to the combination, whereas A/BPO demonstrated superiority. Moreover, a much higher decrease in total inflammatory and non-inflammatory lesion counts was observed in the A/BPO group as early as week 2, while the commencement of action in all other groups was noted to be not earlier than week 4 (BPO group) [31].

EXCIMER LIGHT

Excimer laser/light denotes a category of lasers functioning in the ultraviolet spectrum, used in dermatology as a technique for nonablative selective phototherapy. These are generated by the dissociation of the excited dimer created by a combination of a noble gas and a halide. The 308-nm xenon-chloride excimer laser is the most effective for dermatological applications because it emits a 308-nm monochromatic coherent wavelength within the UV-B band [32].

Excimer is a dimer in an excited state generated by molecular photo-association. Excimers are categorized into two distinct types: dynamic excimers and static excimers. The former results from the collision of ground-state and excited-state molecules, whereas the latter is derived from the photoexcitation of a ground-state dimer formed by weak molecular interactions, like π–π stacking or hydrogen bonding. Excimers may be classified into 2 categories: intermolecular excimers and intramolecular excimers [33].

Mechanism of action:

The excimer light's method of action, comparable to that of UVB radiation, triggers apoptosis in T lymphocytes and keratinocytes. The 308 nm wavelength absorption causes DNA fragmentation, enhances the expression of the tumor suppressor gene p53, and subsequently decreases the proto-oncogene Bcl-2, resulting in cell cycle arrest in T lymphocytes and keratinocytes [34].

Possible role in acne vulgaris treatment:

Data about the efficacy of NB-UVB treatment for AV is very limited. It's been proposed that UVB directly suppresses Cutibacterium acnes and influences the synthesis of inflammatory cytokines. A case study by **Zeichner *et al.*** [35] demonstrated enhancement in inflammatory pustules and papules in a pregnant woman following 2 months of treatment with NB-UVB [35]. A research including 104 individuals indicated that the combination of oral azithromycin and NB-UVB resulted in a greater enhancement of inflammatory papules in contrast to only oral azithromycin [33]. Excimer light is equivalent in terms of efficacy and safety and is better than NB-UVB. The benefits of monochromatic excimer laser therapy compared to NB-UVB include: (a) a reduced irradiation duration, (b) targeted irradiation of limited regions, minimizing malignancy risk and (c) a lower frequency of weekly sessions, advantageous for patients [35].

CONCLUSION

Excimer light therapy seems to be a secure and efficient therapeutic option for AV, with a greater reduction in inflammatory lesions and higher patient satisfaction contrasted to topical adapalene/benzoyl peroxide gel.

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