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An Insight of Use of Topical Adapalene in Management of Post Acne Scars: Review Article

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ABSTRACT

Background: This inflammatory condition affects the pilosebaceous unit, causing comedones, inflammatory papules, and pustules to appear on the face, chest, and back. Propionibacterium acnes and inflammation surrounding the pilosebaceous unit, aberrant keratinization, and increased sebum production all play a role in acne's pathophysiology. Scarring from acne and acne can lead to low self-esteem and feelings of embarrassment, all of which have a negative impact on one's overall wellbeing.

Objective: To see if topical adapalene can help with post-acne scar treatment.

Methods: The databases were searched for articles published in English in 4 data bases [PubMed – Google scholar- Egyptian Knowledge Bank - Science direct] and Boolean operators (AND, OR, NOT) had been used such as topical adapalene and post acne scars OR acne scar treatment and in peer-reviewed articles between January 2000 and March 2021. Documents in a language apart from English have been excluded as sources for interpretation was not found. Papers apart from main scientific studies had been excluded (documents unavailable as total written text, conversation, conference abstract papers and dissertations).

Results: Anti-acne retinoid adapalene (ADP) was licensed by the FDA in 1996 for use in treating acne. It improves the appearance of the skin of the face by reducing facial lesions. Acne lesions, both inflammatory and non-inflammatory, respond well to adapalene gel treatment. In terms of adverse effects, the medicine is completely safe and does not cause burning or dryness.

Conclusion: It is possible that adapalene, which has been shown to be effective in the therapy of photoaging-related skin damage, could have a similar effect on the treatment of atrophic acne scars.

Keywords: Topical adapalene, Post acne scars.

INTRODUCTION

Adolescent acne affects 95–100 percent of 16–17-years-old males and 83–85 percent of 16–17-years-old females, and it remains into adulthood in roughly 12–14 percent of instances [(1)]. Pilosebaceous glands are most prevalent on the face, chest and back, where the prevalence of acne is 92, 45 and 61% respectively. When active acne heals, scarring occurs. This can be produced by any type of acne, from papules, pustules and comedones to the more severe nodulocystic variety [(2)]. There are two types of acne scarring: Atrophic and hypertrophic. Scar types such as boxcar, icepick, and rolling atrophic acne scars influence the therapy options available [(3)].

Many recent evidence-based guidelines for acne have recognized that retinoids play a significant role in this prevalent illness, including those from the AAD and the S3 guidelines from the European Dermatology Forum (EDF) [(4)].

Topical treatment for acne using third-generation retinoid, adapalene, has shown good clinical success. Adapalene offers a superior benefit-to-risk ratio than other retinoids when administered properly [(5)].

The aim of the review was too check whether topical adapalene can help with post-acne scar treatment.

Adapalene: FDA approved Adapalene (ADP) in 1996 for acne therapy (brand name Differin, Galderma) with less side effects than tretinoin (commercial name Retin A) [(6)].

Hair follicle development and maintenance was improved, while melanogenesis was inhibited, both of which were helpful in the therapy of photoaging. For the most part, ADP's anti-proliferative impact has been inadequately characterized, and its mechanism of action has not been thoroughly investigated thus far. Some cancers may benefit from ADP's anti-proliferative properties. In addition to topical ADP and other APIs, innovative treatment combinations with orally given APIs were also described with favorable results. New ADP analogues with therapeutic promise are still a problem to design [(7)].

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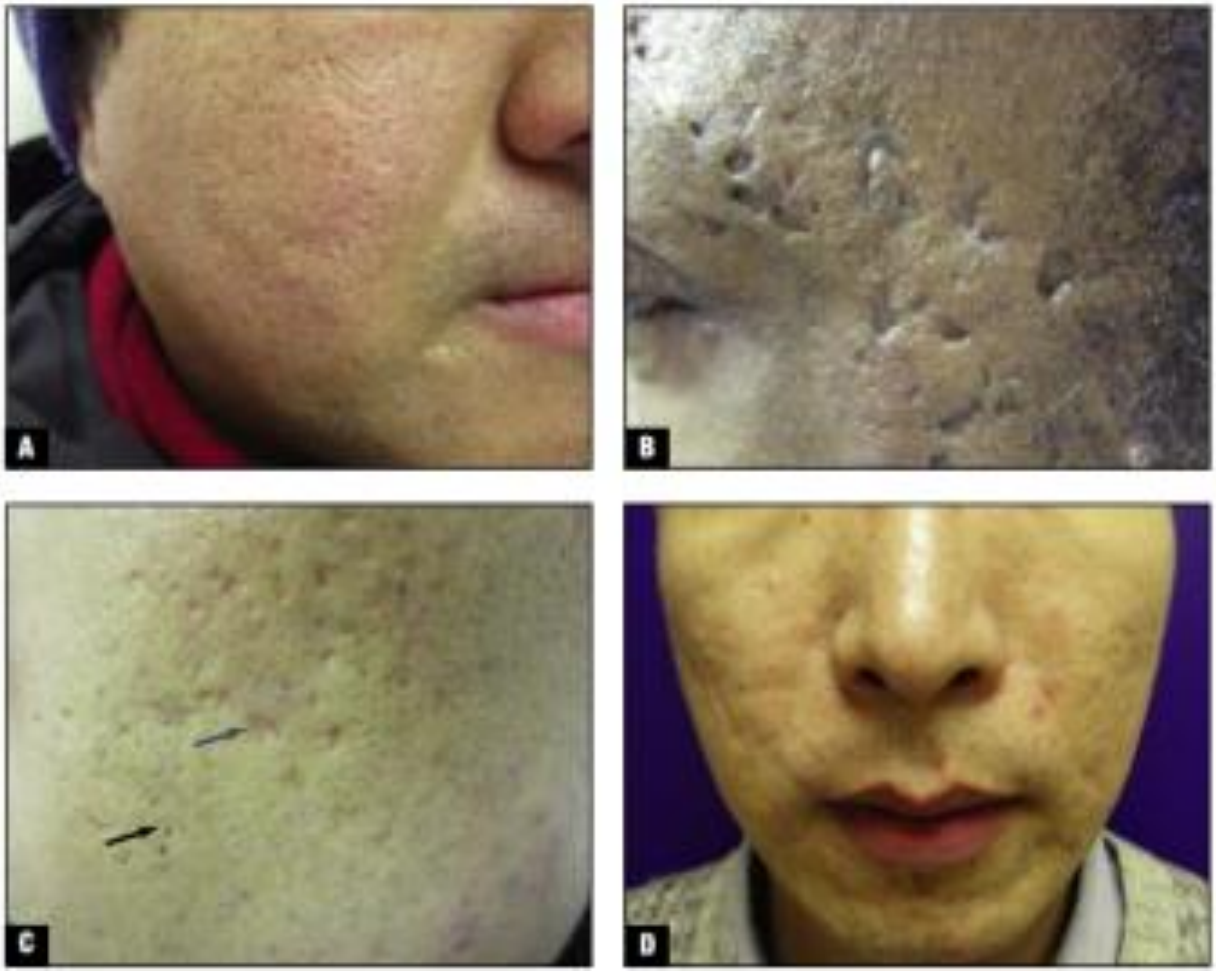

Figure (1): Types of atrophic acne scars. **(A)** Icepick. **(B)** Boxcar. **(C)** Icepick (black arrow) and boxcar (blue arrow). **(D)** Rolling.

Mechanism of action:

Retinoids work by attaching to certain retinoid receptors and causing an effect. RAR-targeting retinoids have an impact on cell differentiation and growth. Additionally, tretinoin and tazarotene, which have been proven to be effective in treating acne, psoriasis and photoaging, fall under this category. Many other retinoids, including alitretinoin and bexarotene, are effective against mycosis fungoides and Kaposi's sarcoma. Thanks to their RXR-targeting properties [(8)].

To activate genes involved in cell development, ADP only binds to RARs and not to retinoic acid's cytosolic binding proteins. RAR- γ receptors, which are found in the epidermis, have a high affinity for ADP. Moreover, dermal fibroblasts are the primary source of RAR- β. Nonetheless, it is not as effective as trifarotene as a RAR- γ agonist [(9)].

Effects:

Acne vulgaris can be treated with ADP. Pilosebaceous cysts, nodules, papules, pustules, and comedones are all signs of acne vulgaris, a chronic inflammatory skin disease. Inflammation, aberrant keratinization of the skin, and increased sebum production are all contributing factors in the pathophysiology of this condition. ADP's efficacy is comparable to that of tretinoin, however it is more stable and lipophilic than the former [(9)].

1. Anti-inflammatory and comedolytic effects:

Wang *et al.* [(7)] reported that comedolytic and anti-inflammatory properties have been established. ADP inhibits arachidonic acid's lipooxygenase and oxidative metabolism, thereby interfering with the inflammatory response. Inflammatory acne may be improved by topical application of ADP therapy, according to the study of the authors.

2. Keratolytic effect:

Acne vulgaris can be treated with ADP or other retinoids to get rid of the aggravating causes and get rid of the acne altogether. Benzoyl peroxide is less keratolytic than 0.1 percent ADP. ADP has been shown to be effective in the treatment of hyperkeratosis. It also has a lower absorption in the corneum layer, resulting in a longer-lasting effect on the epidermis and hair follicle, which is a significant treatment target in acne vulgaris. As a result of the gel's hydration and occlusion action, the medicine is more likely to accumulate in the skin, making it more effective [(10)].

3-Immunomodulatory effect:

Baran and Maibach [11] reported that some retinoids, notably ADP, have been shown to have immunomodulatory properties. Leukotrienes, lipoxygenases, and free radicals generated by polymorphonuclear leukocytes are all inhibited by ADP, which has an immunomodulatory effect (derived from rabbits). Chemoattraction of polymorphonuclear cells and the expression of mammalian toll-like receptor 2 (TLR-2) on human monocytes are also inhibited by the addition of ADP to the culture medium. In addition to targeting RAR receptors, this mode of action is employed.

4. Antiproliferative effect:

All retinoids play an important role in cell development and differentiation, and this is well established. For cervical intraepithelial cancer, ADP proved to be an effective treatment. Treatment of cervical intraepithelial neoplasia at stage 2 with ADP was the most successful [12]. **Shi *et al.*** [13] reports stated that ADP could be used to treat human colon cancer.

5. Neuroprotector effect:

A critical role for retinoid signaling in neurodevelopment and adult CNS function has been established. Dysregulation of retinoid signaling may play a role in some neurodegenerative disorders. ADP-encapsulated nanoparticles were found to be bioactive in the central nervous system (CNS) when delivered intravenously to healthy mice (minimum 24 h). In the future, ADP and retinoid-modulating medicines may be used to treat CNS illnesses [14].

6. Antibacterial activity:

ADP loaded nano-emulsion with tea tree oil was tested for antibacterial efficacy against Propionibacterium acnes. The findings showed that the minimal inhibitory concentration is substantially lower than previously thought. Antibacterial action against methicillin-resistant Staphylococcus aureus may be attributable to adamantane that intercalates into the lipidic bacterial membrane of one analogue of ADP [15].

Adapalene in post-acne scars:

Because both photodamaged skin and atrophic acne scars have lost their dermal matrix, adapalene 0.3 percent may have a comparable effect on atrophic acne scars as it does on photoaging [16].

Percy [17] reported that adapalene 0.1 percent gel was also found to have a substantial impact on the total number of lesions. After a 12-week treatment period, 96.3% of individuals had shown improvement in their acne. 18% had lesions completely cleared, while another 44% showed a great improvement (>75%) in their condition.

Loss *et al.* [16] stated that adapalene 0.3% gel was evaluated for its efficacy, safety, and results were reported by patients with atrophic acne scars. Daily application of an adapalene 0.3 % gel demonstrated good clinical performance, an acceptable tolerability profile, and an improvement in overall well-being in the treatment of atrophic acne scars, according to this study's findings.

Karan *et al.* [4] reported that the efficacy and safety of topical adapalene (0.1%) were investigated and concluded that 0.1% gel is an effective therapy modality for the treatment of both inflammatory and non-inflammatory lesions associated with acne vulgaris in adults. The negative effects of the medicine, which include burning and dryness, are modest.

Side effects:

Acne vulgaris can be effectively treated with ADP-containing topical pharmaceuticals, even by teenagers. ADP is more tolerable than other topical retinoids. Tretinoin is more irritating, hence ADP at 0.1% is preferable than T/I/E in terms of tolerability. ADP's most prevalent side effects include photosensitivity, redness, erythema, dryness, skin irritation, pruritus, desquamation, and stinging/burning, which are all minor adverse reactions. There are noticeable changes in side-effect intensity throughout the course of two weeks of treatment [18].

The time-controlled absorption of the drug and the ADP concentration impact the severity of side effects. Tolerability and acceptance have been taken into consideration in the development of two similar pharmaceutical formulae (0.1% cream and 0.1% lotion). In addition, microsphere ADP gel (0.1%) was better tolerated than ADP gel and maintained the same efficacy. When using ADP gel (0.1%), one patient developed an adverse reaction to the gel [19].

Signs of acute retinoid toxicity are similar to those of vitamin A intoxication. Inflammatory bowel disease flares, hair loss, musculoskeletal pains, changes in serum lipids and transaminases, pseudotumor cerebri, hypothyroidism, and dry skin are all symptoms of dry skin. In contrast to selective RXRs retinoids, which mainly affect the mucosa and musculoskeletal system, selective RARs retinoids are more likely to cause alterations in the body's biochemistry. Anxiety, depression, and mood swings have been linked to oral retinoids, although ADP is a topical retinoid with very little systemic absorption [20].

Retinoids that are taken orally are considered teratogens. Because of this, these substances are not recommended for pregnant women or those who aspire to become pregnant. The danger level associated with consuming ADP is rated as C. (Food and Drug Administration-Pregnancy Categories) [20]. On the other hand, in a paper, tretinoin is deemed safe as an embryotoxic agent because it is applied to the skin [21].

CONCLUSION

It is possible that adapalene, which has been shown to be effective in the therapy of photoaging-related skin damage, could have a similar effect on the treatment of atrophic acne scars.

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