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Topical vitamin D as a new acne treatment. A review of the literature

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ABSTRACT

Acne vulgaris is a common dermatosis with a complicated and multifactorial basis, occurring in adolescent and adult patients. It is a disease of the pilosebaceous unit. Currently, various treatment regimens are used; the therapy is usually long-term and not consistently effective, and the disease tends to recur. Acne often negatively affects the mental health of patients, both in the active phase and after healing. This is caused by the formation of unsightly scars and discolorations. For this reason, we still need modern drugs in therapy. The anti-inflammatory properties of vitamin D3 have long been known. Its topical form is already particularly useful in dermatology in treating psoriasis. This article aims to analyze the literature describing the use and effectiveness of topical vitamin D3 in the treatment of acne vulgaris.

Keywords: Acne vulgaris, topical vitamin D, topical calcitriol, vitamin D deficiency

1. INTRODUCTION

Acne vulgaris (AV) is the most common chronic dermatological disease. It occurs in about 80% of people aged 11-30 and even 100% aged 11-17. 20% of people have moderate or severe acne. Acne lesions may also affect 3% of men and 5% of women over 40 (Bergler-Czop, 2013). It is a disease of the pilosebaceous unit with accompanying seborrhea. It occurs most often on the face and upper torso (Szepietowski et al., 2012; Adamski and Kaszuba, 2019). Acne manifests in skin eruptions such as blackheads, papules, and pustules, which frequently heal and lead to scarring and discoloration (Oge' et al., 2019). Due to its nature, it causes many social complications like low self-esteem and difficulties in interpersonal relationships, which lead to mental disorders (Heng and Chew, 2020). Treatment is both topical and systemic. Therapy is usually long-term and may be accompanied by severe side effects (Podgórska et al., 2021).

2. METHODOLOGY

This article reviews already published literature on the use of topical vitamin D in acne treatment. Using a database of 21 articles, a concise summary was created regarding the potential application of topical vitamin D in treating acne. The literature was sourced from the PubMed database, ResearchGate, and book references, covering publications from January 2007 to September 2024.

3. RESULT AND DISCUSSION

Pathogenesis of acne

The pathogenesis of AV is multifactorial and has not been fully understood. The basis of pathogenesis is: inflammation, seborrhea, keratosis of hair follicles, infection with *Cutibacterium acnes* bacteria and hormonal changes (Sobjanek et al., 2007). A correlation has also been shown between the severity of acne lesions in both sexes and an increased number of androgen receptors on the surface of the sebaceous glands. *Cutibacterium acnes* excrete extracellular products, i.e. lipases, proteases, hyaluronidases and chemotactic factors. This leads to the intensification of inflammatory processes (Dréno et al., 2018). Genetic factors are also among the causes of acne lesions.

People with a positive family history have a fourfold increased risk of developing the disease, its earlier manifestation, the probability of a severe form, and the occurrence of resistance to treatment. The factors responsible for this are probably CYP1A1 - it can lead to retinoid deficiency, causing hyperkeratinization, and CYP17 - the effect on androgen levels. Current acne therapy is mainly based on the local use of retinoids, antibiotics, and benzoyl peroxide. In severe or treatment-resistant forms, oral isotretinoin therapy is recommended. However, it is a drug that potentially causes many adverse effects, and treatment with it is conducted under strict medical supervision (Biegaj, 2017).

The importance of vitamin D deficiency in acne.

Vitamin D deficiency is currently being studied as one of the risk factors for acne. A 2022 meta-analysis on the relationship between acne and serum vitamin D3 levels found reduced levels in people with dermatosis, and a relationship between vitamin D3 levels and the severity of skin lesions was also demonstrated (Hasamoh et al., 2022). Vitamin D3 modulates the immune system, regulates the proliferation and differentiation of keratinocytes and sebocytes, and has antioxidant and anticomedogenic effects. Therefore, its deficiency may be related to the pathogenesis of AV, as evidenced by recent studies (Heng and Chew, 2020; Hasamoh et al., 2022; Naheed et al., 2023; Alhetheli et al., 2020). So far, the topical form of vitamin D3 has been approved by the FDA for treating psoriasis, but its potential use is also being widely studied in the case of other skin diseases (Wat and Dytoc, 2014).

Vitamin D3 has a couple of biological mechanisms as anti-inflammatory. VDR (vitamin D receptor) receptors for this vitamin are present on T and B lymphocytes in their active phase. A particular target seems to be Th cells and indirect modulation of cytokines they produce, such as IL-2, IL-3, IL-4, IL-5, IL-10 IFN- γ , TNF α (Mostafa and Hegazy, 2015). Increased concentrations of IL-1 β , which appears to be a mediator initiating the inflammatory cascade, have also been demonstrated within acne lesions, making it an essential target for vitamin D (Dahlan et al., 2024). It has also been found to reduce the expression of other proinflammatory cytokines, such as IL-6, IL-8, and metalloproteinase (Li et al., 2024). Calcitriol also affects the differentiation and proliferation of skin cells. Suppression of sebaceous gland cell proliferation by vitamin D has also been proven (Agak et al., 2014).

Topical vitamin D in acne treatment

Along with research on the pathogenesis of acne, new methods of its treatment are developing. So far, topical antibiotics, retinoids, benzoyl peroxide, azelaic acid, and salicylic acid are commonly used to treat acne (Lee et al., 2013). Local application of vitamin D is a new method of treatment, but the available literature on this topic is currently limited (Table 1). In a 2024 study, in a group of 33 patients with inflammatory acne in the facial region, thoracic area, and dorsal region due to vitamin D deficiency applied vitamin D locally twice a day (morning and evening), (Lekic and Pavlovic, 2024). They achieved at least a 30% improvement in all patients after a month of using the preparation.

Dahlan et al., (2024) conducted a randomized, double-anonymized, placebo-controlled trial that showed that topical vitamin D3 effectively reduced IL-1 β levels in acne lesions and reduced the severity of inflammatory lesions. Another study by Mahran et al., (2024) involved dividing 60 patients into two groups, one receiving adapalene for one side of the face and calcipotriol for the other, the second group calcipotriol and placebo for one and the other side of the face respectively. The results provided reliable data on the

efficacy and safety of calcipotriol compared with the placebo group (Mahran et al., 2024). Abdel-Wahab et al., (2022) applied calcipotriol cream and adapalene gel to forty patients with AV on the right and left sides of the face, respectively.

After two months of treatment, a significant reduction in skin lesions was observed on both sides of the face, with no significant difference between the right and left sides (Abdel-Wahab et al., 2022). A histological decrease in the density of inflammatory infiltrates was also described, which occurred bilaterally, with a slight advantage in efficacy on the side treated with calcipotriol. Topical calcipotriol may have a significant effect on the course of AV due to its anti-inflammatory effect, which appears to be comparable to the impact of the recognized and widely used topical retinoid, adapalene.

Table 1 Available trials about topic vitamin D in acne.

Author(s), year	Type of trial	Number of participants	Type of intervention	Results
Dahlan et al., 2024	Double-anonymized, randomized, placebo-controlled clinical trial with a 2-arm design	64, divided into two groups	I group - topical vitamin D (cholecalciferol 50 mcg) II group - topical placebo	Significant reduction of acne lesions (p = 0.045), reduction of IL-1β levels within acne lesions (p = 0.028)
Mahran et al., 2024	Triple-blind, randomized, placebo-controlled split-face clinical trial	60, divided into two groups	I group - calcipotriol 0.005% cream on one facial side and placebo over the other side II group - adapalene 0.1% gel over one facial side vs. calcipotriol on the other side	Significant reduction in acne lesions on the calcipotriol-treated side vs. placebo; adapalene remained the best results
Abdel-Wahab et al., 2022	Split face prospective study	40	Topical calcipotriol (0.005%) cream on one facial side and adapalene 0.1% gel over the other side	Significant reduction of acne lesions (p = 0.0001) on both sides with no visual difference between two sides, histologically, a decrease of density of inflammatory infiltrate more significant on the calcipotriol-treated side (p < 0.0001)
Lekic and Pavlovic., 2024	Prospective study	33	Topical cholecalciferol	Reduction in inflammatory acne ranged from 100% to 10% depending on the body area (facial, dorsal, thoracic area) and gender. Overall, improvements were evident in all participants, with none falling below a 30% reduction.

4. CONCLUSION

AV is a serious medical and social problem. It is the most common chronic dermatological disease. In addition to clinical skin symptoms, this disease leads to mental disorders. Knowledge of its causes and exacerbating factors can contribute to introducing new innovative therapies. Treatment aims to reduce the discomfort caused by skin eruptions, improve appearance, and prevent scarring

and discoloration, prevent various adverse psychological effects. Current acne treatment is long-term, complex, and often burdensome for the patient body.

Despite the availability of numerous local and systemic treatment methods, a significant number of patients still struggle to achieve lasting therapeutic efficacy, which is why it is so vital to search for new treatment methods. Studies conducted so far show that local use of vitamin D3 has an effectiveness similar to that of the retinoid adapalene, recognized in standard treatment. Despite the paucity of research and its limitations, we should take a closer look at the use of topical vitamin D3 therapy as an adjunct or alternative to standard acne treatment, as it has significant anti-inflammatory effects and may prove to be an innovative tool in the treatment of this common dermatological condition.

Author contributions

Aleksandra Jonkisz: Conceptualization, writing-rough preparation, investigation

Seweryn Rozalczyk: Visualization, formal analysis, supervision

Justyna Kowalczywska: Writing - Review and editing, supervision

All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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