

THERAPEUTIC EFFICACY OF ISOTRETINOIN IN THE TREATMENT OF ACNE VULGAR: A BIBLIOGRAPHICAL REVIEW

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Abstract: Objective: To analyze the therapeutic efficacy of isotretinoin in the treatment of moderate to severe acne, considering its safety and impact on patients' quality of life. Method: Literature review using the PubMed database, with search terms such as "isotretinoin", "moderate to severe acne", "clinical results and quality of life". 31 articles were analyzed. Results: Acne vulgaris is prevalent in puberty and adolescence, with oral isotretinoin being a primary therapeutic option. Recent studies indicate improvements in quality of life, despite adverse effects such as anxiety, depression and suicidal ideation, related to the severity of acne and a history of psychological conditions. There is no therapy with fully proven efficacy. Final considerations: Oral isotretinoin has favorable clinical results and improved self-esteem, but more research is needed to benefit patients with moderate to severe acne.

Keywords: isotretinoin, acne vulgaris, quality of life, safety, treatment.

INTRODUCTION

Acne vulgaris is an inflammatory dermatological condition that predominantly affects the sebaceous follicles of adolescents and young adults, presenting with a variety of lesions, including comedones, inflammatory papules, pustules, nodules, cysts and disseminated scars. The pathogenesis of acne is complex, involving increased sebum production, influenced by hyperstimulation or hypersensitivity to androgens, such as dihydrotestosterone (DHT) and testosterone. These hormones stimulate the sebaceous glands to secrete interleukin (IL)-1, which triggers inflammation and epithelial hyperkeratinization. Additionally, follicular colonization by *Cutibacterium acnes* (*C. acnes*) is considered a crucial factor in the pathogenesis of acne (Ma et al., 2022).

The prevalence of acne is particularly high, affecting around 70% of girls and 73% of boys between the ages of 9 and 12, with skin sensitivity in this age group contributing to this statistic. In adolescents and young adults, the prevalence reaches up to 85%, remaining high until around 25 years of age, after which the incidence declines to approximately 10%. Although many patients experience spontaneous resolution after puberty, acne can persist beyond age 25 and, in rare cases, until age 40 (Ma et al., 2022).

In recent years, there has been a significant increase in the use of oral isotretinoin, known as 13-cis-retinoic acid or ISO, for the treatment of severe acne, especially in the nodulocystic form. Isotretinoin is effective in influencing all the main pathogenetic factors of acne: it suppresses the secretion of sebaceous glands, normalizes keratinization, reduces the proliferation of *C. acnes* and exhibits anti-inflammatory properties. This increase in isotretinoin use, particularly notable between 2013 and 2019, reflects increasing restrictions on the use of oral antibiotics, driven by the need to mitigate the risk of developing bacterial resistance (Mobacken, 2021; Skroza et al., 2021).

With the rising costs of dermatological medications and greater cost-sharing by patients due to high-deductible health plans, the search for cost-effective treatments intensifies. Generic adapalene benzoyl peroxide in a fixed dose, clindamycin-BPO in a fixed dose, and hormonal agents such as combined oral contraceptives and spironolactone are cost-effective alternatives, especially for patients with mild to moderate acne. Doxycycline and isotretinoin also stand out as economical options for treating more severe forms of acne (Shields; Barbieri, 2023).

The objective of this literature review is to analyze and synthesize recent studies on the therapeutic efficacy of isotretinoin in the

treatment of moderate to severe acne, also examining the safety and impact on patients' quality of life. This study seeks to provide a comprehensive overview of emerging therapeutic strategies and their impact on the clinical management of acne.

METHODOLOGY

The present study constitutes a bibliographical review prepared according to the strategy of PVO, adapted to include: Population or research problem, intervention, variables and Outcome. This methodology was applied to investigate the following guiding question: "What is the current evidence on the use of isotretinoin in the treatment of moderate to severe acne, and how does this therapy influence clinical results and patients' quality of life?"

The searches were conducted in the PubMed- MEDLINE (Medical Literature Analysis and Retrieval System Online) database, using the terms "isotretinoin", "moderate to severe acne", and "clinical results and quality of life", combined with the Boolean operators "AND" and "OR". This initial strategy identified a total of 561 articles.

The inclusion criteria adopted were: articles published between April 2019 and November 2023 that directly addressed the topics of interest, including systematic review studies, randomized clinical trials and case-control studies, all available in full. On the other hand, duplicate articles, those published only in summary form, and those that did not directly address the established research question or that failed in meeting the other inclusion criteria.

After applying the inclusion and exclusion criteria, the final selection was restricted to 31 relevant articles available in the PubMed database. These documents form the basis for the analysis and discussion that make up the main body of the present study. This

methodological approach allowed for a rigorous and up-to-date assessment of the available evidence on the efficacy and impact of isotretinoin in the treatment of moderate to severe acne, focusing both in clinical results and in the quality of life of affected patients.

DISCUSSION

IMPACT ON QUALITY OF LIFE AND PSYCHOSOCIAL OUTCOMES

Acne vulgaris is a dermatological condition prevalent mainly during puberty, adolescence and youth, affecting more than 5 billion people around the world (Mavranouzouli et al., 2022). Among the various therapeutic options available, oral isotretinoin (13-cis-retinoic acid) stands out as the most effective and widely studied first-line drug for cases of moderate to severe acne, especially in nodular-cystic and drug-resistant conditions. conventional therapy (Kapala et al., 2022).

The 13-cis-retinoic acid, a retinoid derived from vitamin A, acts comprehensively on the etiopathogenic factors of acne vulgaris. It is the only known monotherapy capable of inducing prolonged remission or cure in up to 80% of patients after a single cycle of treatment (Bagatin et al., 2020). Recent research has revealed that, in addition to clinical benefits, isotretinoin can also significantly improve patients' quality of life, despite reports of adverse psychological effects such as anxiety, social inhibition, depression and suicidal ideation associated with the use of the medication (Bagatin et al., 2020).

In the United States, isotretinoin is often associated with reports of depression and suicide attempts. It is important to note that the risk of psychosocial repercussions may be related to the severity of acne, the number and type of lesions, as well as the presence of scars and sequelae (Kapala et al., 2022). The choice of treatment must be decided together

with the patient, taking into consideration, personal preferences, as well as the risks and benefits of each option (Mavranouzouli et al., 2022).

It is possible that certain subgroups of patients, especially those with a prior history of psychological conditions, are more susceptible to developing drug-induced depression or psychosis. However, current evidence is not sufficient to completely contraindicate its use. Therefore, the prescription of isotretinoin must carefully consider the individual's clinical history, evaluating the relationship between treatment efficacy and safety (Laurent et al., 2023).

The patient's understanding of potential adverse effects is essential to minimize treatment interruption and possible future complications. Common mucocutaneous side effects include dry skin, skin fragility, dermatitis, erythema, xerosis, rashes, dry and cracked lips, dry and painful mouth, excessive thirst, and cheilitis. These symptoms, although reversible, require regular clinical monitoring to mitigate risks (Kapala et al., 2022).

Finally, despite advances in research into the treatment of acne vulgaris, there is still no therapy with completely proven effectiveness. However, it is observed that the use of oral isotretinoin has demonstrated favorable clinical results, improving self-esteem and mitigating the negative impacts on patients' psychological and social well-being.

EFFICACY AND SAFETY OF ISOTRETINOIN IN THE TREATMENT OF MODERATE AND SEVERE ACNE

Over the past five years, a number of studies have focused on the effectiveness and safety of isotretinoin in treating moderate to severe acne. Currently, this drug is widely recommended for affected patients, largely due to concerns about its potential adverse effects. Review of these studies indicates that isotretinoin demonstrates a positive therapeutic profile, particularly effective in severe cases and at higher cumulative dosages (100–120 mg/kg, >120 mg/kg). Such findings are corroborated by Skroza et al. (2021) and Jorgaqi et al. (2020), who report a significant improvement in Global Acne Grading System (GAGS) scores and superior efficacy compared to treatments combining antibiotics, topical retinoids, and benzoyl peroxide.

Recent research also explores innovative treatment combinations, such as low-dose isotretinoin therapy plus Pulsed Dye Laser (PDL), which has shown superior results when compared to higher-dose isotretinoin monotherapy (Ibrahim et al., 2021). Additionally, it was discovered that isotretinoin negatively modulates the levels of the S100a7a protein, which contributes to a better understanding of its mechanisms of action (Al-Sudany; Mohammed; Alrifai, 2019).

Regarding the safety of isotretinoin, recent studies focus on teratogenicity and other serious side effects such as liver changes, dry eyes, arthralgia, and psychological changes, including depression (Vasam, Korutla, and Bohara, 2023; Chen, Li, Li, and Chen, 2020). To mitigate such risks, it is suggested to modulate doses or develop formulations that maintain therapeutic efficacy with an improved safety profile. Studies such as those by Bagatin et al. (2020) indicate that dosage

adjustments to 0.1-0.5 mg/kg, extending the duration of treatment for up to 18 months, can significantly reduce adverse effects.

Considering the restriction of the use of isotretinoin in patients with depression or pregnancy, the importance of strict monitoring protocols to detect and manage symptoms of depression is noted, minimizing the risk of suicide. Despite precautions, studies such as that by Laurent et al. (2023) indicate that patients treated with isotretinoin may have a lower suicide attempt rate than that observed in the general population, suggesting an association between the severity of acne and the occurrence of psychiatric disorders.

FINAL CONSIDERATIONS

Acne vulgaris in moderate to severe stages can have major negative repercussions on the patient's life, both dermatological and psychological, correlated with its severity. In these cases, the first-line drug is oral isotretinoin. However, it is crucial to emphasize the need for more research into its psychological repercussions, as studies demonstrate improvements in self-esteem, associated with the psychological and social well-being of patients, but also point out the risk of developing depression or psychosis, especially in patients with a history prior psychological condition. Furthermore, previously healthy patients may experience anxiety, social inhibition, depression and suicidal ideation. In summary, this literature review aims to summarize recent studies on oral isotretinoin therapy in the treatment of moderate to severe acne and propose new research that benefits these patients in terms of mental health and well-being.

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