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Original Article

Comparison of Efficacy and Safety of High-Dose Isotretinoin Versus Low-Dose Isotretinoin with Pulsed Oral Azithromycin in Moderate to Severe Acne Vulgaris

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Abstract

Objective: To evaluate and compare the efficacy and safety of high-dose isotretinoin with low-dose isotretinoin combined with pulsed oral azithromycin in patients with moderate to severe acne vulgaris.

Methodology: This comparative clinical study included patients diagnosed with moderate to severe acne based on the Global Acne Grading Score (GAGS). Participants were divided into two treatment groups:Group A (31 patients) received high-dose isotretinoin, while Group B (31 patients) received low-dose isotretinoin with pulsed oral azithromycin.Patients were followed monthly, and outcomes were assessed in terms of reduction in GAGS and incidence of adverse effects.

Results: Both treatment regimens resulted in significant clinical improvement. High-dose isotretinoin demonstrated a faster and more pronounced reduction in acne severity. However, the combination regimen achieved comparable overall improvement with a lower frequency of adverse effects.

Conclusion: Low-dose isotretinoin combined with pulsed azithromycin provides an effective and better-tolerated alternative without significant side effects and being cost-effective, whereas high-dose isotretinoin remains superior for rapid clinical clearance.

Keywords: Acne vulgaris, isotretinoin,azithromycin, combination therapy, GAGS

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Introduction

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit and represents one of the most common dermatological conditions worldwide. It affects approximately 80-85% of adolescents and may persist into adulthood, particularly in females.[1] The condition arises from a complex interplay of increased sebum production, abnormal follicular keratinization, colonization with Cutibacterium acnes, and inflammatory cascades.[2]

The clinical spectrum of acne ranges from comedonal lesions to inflammatory papules, pustules, nodules,and cysts. In moderate to severe cases, acne can leadto permanent scarring and significant psychosocial morbidity,including anxiety, depression, and reduced self-esteem. Therefore, effective and timely treatment is crucial.[3]

Oral isotretinoin has revolutionized acne management due to its ability to target all major pathogenic mechanisms.It reduces sebaceous gland size and activity, normalizes keratinization, decreases microbial colonization, and exerts anti-inflammatory effects.[4] Despite its efficacy, isotretinoin is associated with dose-dependent adverse effects, including mucocutaneous dryness, hepatotoxicity, hyperlipidemia, and teratogenicity. These concerns often limit patient compliance and physician preference for higher doses.[5]

To overcome these limitations, alternative regimens have been explored, including low-dose isotretinoin and combination therapies. Azithromycin, a macrolide antibiotic, possesses both antimicrobial and anti-inflammatory properties and has been used in pulsed regimens to enhance therapeutic outcomes while minimizing toxicity. This study was conducted to compare the efficacy and safety of high-dose

isotretinoin with a combination regimen of low-dose isotretinoin and pulsed oral azithromycin in patients with moderate to severe acne vulgaris.

Methods

This comparative clinical study was conducted at a tertiary care dermatology department after obtaining ethical approval. Total 62 patients presenting with moderate to severe acne vulgaris were enrolled after informed consent. All patients aged ≥16 years and suffering from moderate to severe acne (based on GAGS) were included in this study while patients bearing current pregnancy or lactation, having known liver disease, history of hypersensitivity to study drugs or on recent use of systemic isotretinoin were excluded.

Participants were divided into two groups: Group A: High-dose isotretinoin (31), Group B: Low-dose isotretinoin with pulsed oral azithromycin (31). Patients received treatment according to standard dosing protocols for a period of 3 months . Follow-up visits were conducted monthly to assess clinical response and monitor adverse effects. Primary outcome was to observe reduction in GAGS score and secondary outcomes was to observe eduction in lesion count and incidence of adverse effects

Data were analyzed using appropriate statistical methods. Mean changes in GAGS scores were compared between groups, and significance was determined using standard tests.

Results

A total of 62 patients completed the study protocol. .Baseline characteristics were comparable between the two groups. Both treatment regimens resulted in progressive improvement over the study period. Group A (High-dose isotretinoin) showed rapid reduction in inflammatory and non-inflammatory lesions and presented significant decline in GAGS within early follow-up visits while higher frequency of mucocutaneous side effects were observed. Group B (Low-dose isotretinoin with pulsed azithromycin) showed Gradual but consistent improvement, significant reduction in acne severity by the end of treatment and better tolerability with fewer reported adverse effects. Overall, the difference in the rate of improvement favored high-dose isotretinoin, whereas safety outcomes favored the combination regimen.



Figure 1: *Before and after treatment differences among Groups.*

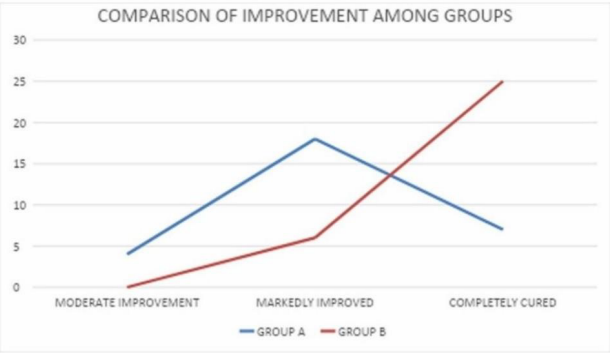


Figure 2: *Comparison of Improvement Among Groups.*

Discussion

The findings of this study demonstrate that both high-dose isotretinoin and a combination of low-dose isotretinoin with pulsed oral azithromycin are effective in the management of moderate to severe acne vulgaris. However, notable differences were observed in the rate of clinical response and safety profiles between the two regimens. High-dose isotretinoin showed a more rapid and pronounced reduction in acne severity. This is consistent with its well-established mechanism of action, particularly its potent sebosuppressive effect and ability to significantly reduce Cutibacterium acnes colonization. Previous studies have similarly reported faster clearance rates with higher cumulative doses, supporting its role as the most effective monotherapy for severe acne.[6,7]

Despite its superior efficacy, high-dose isotretinoin

was associated with a higher incidence of adverse effects, most commonly mucocutaneous dryness, cheilitis, and laboratory abnormalities. These findings align with existing literature that highlights the dose-dependent nature of isotretinoin toxicity.[8] Such adverse effects may affect patient adherence and necessitate dose adjustments or discontinuation in certain cases.

In contrast, the combination regimen of low-dose isotretinoin with pulsed oral azithromycin demonstrated a more gradual but steady improvement. The reduced isotretinoin dose likely contributed to the improved tolerability observed in this group. The addition of azithromycin may have enhanced therapeutic outcomes through its dual antimicrobial and anti-inflammatory effects, which are particularly beneficial in inflammatory acne.

Comparable studies have suggested that low-dose isotretinoin regimens can achieve satisfactory clinical outcomes with fewer side effects, although they may require longer treatment durations.[9,10] The present findings support this approach, indicating that combination therapy can serve as a practical alternative for patients who are unable to tolerate higher doses of isotretinoin.

From a clinical perspective, the choice between these regimens should be guided by individual patient factors, including severity of acne, risk of adverse effects, patient preference, and need for rapid improvement. High-dose isotretinoin may be preferred in cases requiring quick clearance, while the combination regimen may be more suitable for long-term management with improved safety.

Conclusion

Both high-dose isotretinoin and low-dose isotretinoin combined with pulsed oral azithromycin are effective treatment options for moderate to severe acne vulgaris. High-dose isotretinoin provides faster clinical improvement but is associated with a higher incidence of adverse effects. The combination regimen offers a safer and well-tolerated alternative with satisfactory efficacy. Individualized treatment selection remains essential to optimize outcomes.

Ethical Approval: The IRB/EC approved this study via letter no. 11093/REG/KEMU/2016, dated November 28, 2016.

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Authors' Contribution

SS: Conception.

AG: Design of the work.

WN, MS, FNA: Data acquisition, analysis, or interpretation.

AG,WN, MS, FNA: Draft the work.

SS: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

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