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ASSESSMENT OF THE THERAPEUTIC EFFECTIVENESS AND ADVERSE EFFECTS OF ORAL ISOTRETINOIN VERSUS TOPICAL RETINOIDS IN THE TREATMENT OF MODERATE TO SEVERE ACNE VULGARIS

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Abstract

Background: *Acne vulgaris is a common chronic dermatological condition that affects adolescents and adults, often leading to psychological distress and physical scarring. Management typically involves topical or systemic retinoids, but concerns remain regarding their comparative effectiveness and side effect profiles.*

Objectives: *To assess the therapeutic effectiveness and adverse effects of oral isotretinoin versus topical retinoids in the treatment of moderate to severe acne vulgaris.*

Study Design & Setting: *A randomized, comparative clinical trial conducted at the Dermatology Department of DHQ Teaching Hospital Mirpur AJK from November 2024 to April 2025.*

Methodology: *A total of 120 patients aged 15–35 years with moderate to severe acne were randomized into two groups (n = 60 each). Group A received oral isotretinoin (0.5 mg/kg/day) and Group B received topical retinoids (adapalene 0.1% gel or tretinoin 0.05% cream) for 16 weeks. Effectiveness was assessed using percentage reduction in lesion count and change in Global Acne Grading System (GAGS) score. Adverse effects were recorded throughout the study. Data were analyzed using SPSS v25 with $p \leq 0.05$ considered significant.*

Results: *Group A showed a significantly greater reduction in lesion count (82.5% ± 8.3%) and lower GAGS scores (5.2 ± 2.1) compared to Group B (61.4% ± 10.7%, GAGS 10.7 ± 3.4) ($p < 0.001$). Adverse effects like cheilitis and dry skin were more common in Group A, while local irritation was more frequent in Group B.*

Conclusion: *Oral isotretinoin is more effective than topical retinoids in treating moderate to severe acne but is associated with more systemic adverse effects.*

INTRODUCTION

Acne vulgaris is a prevalent chronic inflammatory skin disorder that predominantly affects adolescents and young adults, with a global prevalence of approximately 9.4%, making it the eighth most common disease worldwide (1). The pathogenesis of acne is multifactorial, involving increased sebum production, follicular hyperkeratinization, colonization by Cutibacterium acnes, and subsequent inflammatory responses (2).

Topical retinoids, such as adapalene and tretinoin, are commonly prescribed for mild to moderate acne. These agents function by modulating epithelial cell differentiation, reducing follicular occlusion, and exerting anti-inflammatory effects (3). Recent advancements have introduced trifarotene, a fourth-generation retinoid with selective affinity for retinoic acid receptor gamma, demonstrating efficacy in both facial and truncal acne (4). While topical retinoids are generally well-tolerated, they may cause local adverse effects such as erythema, dryness, and peeling (5).

For moderate to severe cases, oral isotretinoin remains the most effective monotherapy. It targets all major pathogenic factors of acne, including sebaceous gland suppression, normalization of follicular keratinization, inhibition of C. acnes, and anti-inflammatory actions (6). Clinical studies have consistently demonstrated its superior efficacy in reducing lesion counts and achieving long-term remission (7).

However, isotretinoin's use is associated with a spectrum of adverse effects. Common side effects include mucocutaneous dryness, cheilitis, and photosensitivity (8). More severe but less frequent adverse events encompass hepatotoxicity, dyslipidemia, musculoskeletal symptoms, and potential psychiatric effects such as mood alterations and depression (9,10). The teratogenic risk necessitates strict contraceptive measures during and after treatment in women of childbearing potential (11).

Given the efficacy and side effect profiles of both treatment modalities, a comparative assessment is essential to guide clinical decision-making. This study aims to evaluate the therapeutic effectiveness and adverse effects of oral isotretinoin versus topical retinoids in the management of moderate to severe acne vulgaris. The findings will inform evidence-based treatment strategies, balancing efficacy with safety and patient quality of life considerations.

MATERIALS AND METHODS

This comparative, randomized clinical study was conducted at the Dermatology Outpatient Department of DHQ Teaching Hospital Mirpur AJK from November 2024 to April 2025.after obtaining approval from the Institutional Review Board and informed written consent from all participants. A total of 120 patients, aged between 15 and 35 years, clinically diagnosed with moderate to severe acne vulgaris according to the Global Acne Grading System (GAGS), were enrolled using a non-probability consecutive sampling technique.

Sample size was calculated using OpenEpi software, taking a confidence level of 95%, power of 80%, and anticipated difference of 20% in treatment efficacy between groups, yielding a minimum requirement of 60 participants in each group. Patients were randomly allocated into two equal groups (Group A and Group B), each consisting of 60 patients, using a computer-generated randomization list. Group A received oral isotretinoin at a dose of 0.5 mg/kg/day for 16 weeks, while Group B was treated with topical retinoids (either adapalene 0.1% gel or tretinoin 0.05% cream once daily at night) for the same duration. Patients with contraindications to retinoid therapy, pregnant or lactating females, individuals with a history of psychiatric illness, liver dysfunction, or dyslipidemia were excluded from the study.

Baseline demographic data, including age, gender, duration of acne, and baseline GAGS scores were recorded. Follow-up evaluations were conducted at 4-week intervals up to 16 weeks, and effectiveness was assessed based on the percentage reduction in total acne lesion count and improvement in GAGS score. Adverse effects were documented at each visit based on patient-reported symptoms and clinical examination.

Data were entered and analyzed using SPSS version 25. Quantitative variables like age and lesion count were expressed as mean ± standard deviation, while qualitative variables such as gender and side effects were presented as frequencies and percentages. Independent sample t-test and chi-square test were

applied where appropriate, with p-value ≤ 0.05 considered statistically significant.

RESULTS

Both groups were comparable at baseline with no statistically significant differences observed in demographic or clinical characteristics. The mean age of participants in the isotretinoin group was 21.7 ± 4.2 years, while it was 22.3 ± 3.8 years in the topical retinoids group (p = 0.428). Male participants constituted 46.7% in Group A and 50.0% in Group B (p = 0.712). The mean duration of acne was 14.6 ± 5.1 months in the isotretinoin group and 13.9 ± 6.4 months in the topical group (p = 0.561). Baseline Global Acne Grading System (GAGS) scores were also similar between the groups, with a mean of 27.4 ± 3.7 in Group A and 26.9 ± 4.1 in Group B (p = 0.479). At week 16, Group A (oral isotretinoin) showed significantly greater clinical improvement compared to Group B (topical retinoids). The mean percentage reduction in lesion count was 82.5 ± 8.3% in the isotretinoin group versus 61.4 ± 10.7% in the topical group (p < 0.001). The mean Global Acne Grading System (GAGS) score at week 16 was lower in the isotretinoin group (5.2 ± 2.1) than in the topical group (10.7 ± 3.4), indicating better disease control (p < 0.001) given in table 3.

Complete clearance of acne was achieved in 60% (n = 36) of patients in the isotretinoin group, compared to 23.3% (n = 14) in the topical group (p < 0.001). Partial improvement was noted in 33.3% (n = 20) of isotretinoin users and 56.7% (n = 34) of topical retinoid users (p = 0.004). A higher proportion of patients in the topical group (20%, n = 12) experienced no significant response compared to the isotretinoin group (6.7%, n = 4), which was statistically significant (p = 0.030) given in table 2.

During the treatment period, cheilitis was significantly more common in the isotretinoin group, affecting 75% (n = 45) of patients compared to 10% (n = 6) in the topical retinoids group (p < 0.001). Similarly, dry skin was reported in 63.3% (n = 38) of patients receiving isotretinoin versus 20% (n = 12) in the topical group (p < 0.001). Photosensitivity occurred more frequently in Group A (36.7%, n = 22) than in Group B (16.7%, n = 10) with statistical significance (p = 0.010). Elevated liver enzymes were observed in 6.7% (n = 4) of patients on isotretinoin, whereas none in the topical group experienced this adverse effect (p = 0.041). Mood changes were noted in 5% (n = 3) of the isotretinoin group, but this difference was not statistically significant (p = 0.078). Conversely, local irritation was much more prevalent in the topical retinoids group, reported by 40% (n = 24) of patients compared to 1.7% (n = 1) in the isotretinoin group (p < 0.001) (given in table 3).

Table 1: Baseline Demographic Characteristics of Study Participants (n = 120)

Characteristic	Group A (Isotretinoin) n = 60	Group B (Topical Retinoids) n = 60	p-value
Age (years), mean ± SD	21.7 ± 4.2	22.3 ± 3.8	0.428
Gender			
Male	28 (46.7%)	30 (50.0%)	0.712
Female	32 (53.3%)	30 (50.0%)	
Duration of Acne (months),	14.6 ± 5.1	13.9 ± 6.4	0.561
Baseline GAGS Score	27.4 ± 3.7	26.9 ± 4.1	0.479

Table 2: Clinical Response at Week 16 (n = 120)

Outcome	Group A (Isotretinoin) n = 60	Group B (Topical Retinoids) n = 60	p-value
Mean % Reduction in Lesion Count	82.5 ± 8.3	61.4 ± 10.7	<0.001
Mean GAGS Score at Week 16	5.2 ± 2.1	10.7 ± 3.4	<0.001
Complete Clearance	36 (60%)	14 (23.3%)	<0.001
Partial Improvement	20 (33.3%)	34 (56.7%)	0.004

No Significant Response	4 (6.7%)	12 (20%)	0.030

Table 3: Adverse Effects Observed During Treatment (n = 120)

Adverse Effect	Group A (Isotretinoin)	Group B (Topical Retinoids)	p-value
Cheilitis	45 (75%)	6 (10%)	<0.001
Dry Skin	38 (63.3%)	12 (20%)	<0.001
Photosensitivity	22 (36.7%)	10 (16.7%)	0.010
Elevated Liver Enzymes	4 (6.7%)	0 (0%)	0.041
Mood Changes	3 (5%)	0 (0%)	0.078
Local Irritation	1 (1.7%)	24 (40%)	<0.001

DISCUSSION

Acne vulgaris is a chronic inflammatory skin disorder commonly affecting adolescents and young adults. It significantly impacts quality of life due to its visible appearance and potential for scarring. Treatment options vary based on severity, ranging from topical agents to systemic medications.[11] Retinoids, both topical and oral, are widely used due to their comedolytic and anti-inflammatory properties. Oral isotretinoin is highly effective for moderate to severe acne but associated with systemic side effects. Comparative assessment is essential to balance efficacy with safety in acne management strategies.[12]

In our study, oral isotretinoin demonstrated significantly higher clinical efficacy compared to topical retinoids, with a mean reduction in lesion count of 82.5% versus 61.4% ($p < 0.001$), and a mean Global Acne Grading System (GAGS) score at week 16 of 5.2 ± 2.1 versus 10.7 ± 3.4, respectively. These findings are in line with the observations of Vallerand et al. (2018), who reviewed 11 trials involving 760 patients and concluded that isotretinoin consistently reduced acne lesion counts more effectively than placebo or alternative treatments, albeit with a higher incidence of adverse effects.[20] Similarly, Truchuelo et al. (2015) reported improved lesion counts and superior tolerance with isotretinoin therapy, despite patients not always reaching the full cumulative dose.[13]

Our results also align with Bener et al. (2009), who observed marked or complete improvement in 51.9% of patients treated with isotretinoin.[14] The 60% complete clearance rate in our isotretinoin group reinforces the role of isotretinoin in achieving sustained remission. Likewise, Naqvi et al. (2020) found isotretinoin pulse and continuous therapies to be equally effective across acne severities, with efficacy rates as high as 92% in moderate acne.[18]

Contrastingly, Asilian et al. (2024) reported no significant difference in improvement rates between two isotretinoin-based regimens, with overall improvement of 88.36% versus 90.31% ($p = 0.609$), although GAGS score reduction was statistically significant between the groups ($p = 0.006$).[17] These findings suggest that while isotretinoin remains effective, adjunctive strategies may further influence outcomes.

Our study also confirmed the higher frequency of systemic side effects with oral isotretinoin. Cheilitis was observed in 75% of patients, dry skin in 63.3%, and photosensitivity in 36.7%. These side effects were consistent with those reported by Vallerand et al., who documented 751 adverse events with isotretinoin, the majority related to skin dryness.[20] Tahir et al. also observed that although 100% of patients improved with isotretinoin, all experienced some form of adverse effect, leading to discontinuation in two cases.[19] Similarly, Sitohang et al. (2020) emphasized the need for regular clinical assessment and monitoring due to the broad spectrum of isotretinoin-associated side effects.[16]

On the other hand, Ekore et al. (2023) and Bener et al. (2009) highlighted the beneficial role of topical retinoids and reported fewer systemic adverse events, although the efficacy was generally lower than isotretinoin.[14,15] The 23.3% complete clearance and 56.7% partial improvement in our topical retinoid group underscore their suitability for patients unable to tolerate systemic agents.

While our findings affirm the superior efficacy of oral isotretinoin in treating moderate to severe acne vulgaris, they also highlight its higher adverse effect

burden, necessitating individualized treatment decisions based on severity, patient preference, and safety considerations. This study provides a direct comparison of clinical outcomes and side effect profiles between oral isotretinoin and topical retinoids in a well-defined population. Randomization minimized selection bias, and standardized evaluation tools ensured consistency. Adequate follow-up duration allowed for assessment of both therapeutic response and adverse effects. However, the study was limited by its single-center design and moderate sample size. Self-reported adherence may have introduced response bias, especially in the topical group. Laboratory monitoring was limited to liver enzymes and did not include lipid profiles.

CONCLUSION

Oral isotretinoin demonstrated superior clinical efficacy compared to topical retinoids in the treatment of moderate to severe acne vulgaris. However, it was associated with a higher incidence of systemic adverse effects. Treatment selection should be individualized, balancing effectiveness with safety considerations.

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