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COMPARATIVE EFFICACY AND SAFETY OF TOPICAL TRIFAROTENE VERSUS ADAPALENE IN MILD-TO-MODERATE ACNE VULGARIS: A PROSPECTIVE COMPARATIVE STUDY

Dermatology

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ABSTRACT

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit that commonly affects adolescents and young adults. Topical retinoids are a cornerstone of acne treatment due to their comedolytic and anti-inflammatory effects. Trifarotene, a fourth-generation selective retinoic acid receptor-gamma agonist, is a newer topical retinoid with promising efficacy; however, comparative data with adapalene in Indian patients remain limited. This prospective comparative study evaluated the efficacy and safety of topical trifarotene and adapalene in 40 patients with Grade I and Grade II acne vulgaris. Participants received either trifarotene or adapalene once daily and were assessed at baseline, 2, 4, and 6 weeks. Efficacy was evaluated using changes in comedone count, papule count, and total lesion count, while adverse effects were monitored throughout the study. Both treatments produced significant reductions in acne lesions ($p<0.001$). However, trifarotene showed greater reductions in comedones (44.93% vs 32.77%), papules (45.66% vs 29.73%), and total lesion count (45.05% vs 31.87%) compared with adapalene. Adverse effects, including dryness, erythema, scaling, and burning sensation, were mild and comparable between groups ($p=0.216$). These findings suggest that topical trifarotene is more effective than adapalene in managing mild-to-moderate acne vulgaris while maintaining a similar safety profile.

KEYWORDS

Acne Vulgaris; Trifarotene; Adapalene; Topical Retinoids

INTRODUCTION

Acne vulgaris is a common chronic inflammatory disorder of the pilosebaceous unit that primarily affects adolescents and young adults, often causing psychological distress, scarring, and post-inflammatory pigmentation.[1] It affects nearly 80–90% of adolescents and may persist into adulthood.[2] The pathogenesis of acne is multifactorial, involving increased sebum production, follicular hyperkeratinization, colonization by Cutibacterium acnes, and inflammation.[3] Hormonal, genetic, environmental, and lifestyle factors also contribute to disease development and severity.[4]

Topical retinoids are considered the cornerstone of acne management because of their comedolytic, anti-inflammatory, and anti-keratinizing properties.[6] They normalize follicular epithelial desquamation, prevent microcomedone formation, and enhance the efficacy of other topical therapies.[7] Adapalene, a third-generation synthetic retinoid, is widely used in mild-to-moderate acne due to its proven efficacy and favorable tolerability profile.[8] Comparative studies have shown that adapalene provides efficacy comparable to tretinoin while causing less irritation and improving patient compliance.[9]

Trifarotene is a fourth-generation topical retinoid that selectively targets retinoic acid receptor-gamma (RAR-γ), the predominant receptor subtype in the epidermis.[10] This selective activity may improve therapeutic efficacy while minimizing adverse effects.[11] In 2019, trifarotene became the first new topical retinoid approved by the United States Food and Drug Administration for acne vulgaris in nearly two decades.[12] Clinical studies have demonstrated significant reductions in both inflammatory and non-inflammatory lesions with good long-term tolerability.[13] However, comparative studies between trifarotene and adapalene, particularly in the Indian population, remain limited. Therefore, the present study was undertaken to compare the efficacy and safety of topical trifarotene and topical adapalene in the treatment of mild-to-moderate acne vulgaris.

MATERIALS AND METHODS

A prospective randomised comparative study was conducted in the Department of Dermatology, Venereology and Leprology at J.J.M. Medical College and associated tertiary care hospitals, Davangere, Karnataka, from June 2024 to May 2025. Institutional Ethics Committee approval was obtained, and written informed consent was secured from all participants.

A total of 40 patients aged above 12 years with clinically diagnosed Grade I or Grade II acne vulgaris were enrolled using convenience sampling technique from patients presenting to dermatology outpatient department. Patients who had received topical or systemic anti-acne therapy within the preceding two months, pregnant or lactating women, those with Grade III or IV acne, immuno-suppression, or unwillingness to participate were excluded.

Participants were randomly allocated into two treatment groups: Group A received topical trifarotene once daily at night , while Group B received topical adapalene once daily at night.To minimize irritation, week 1 featured a progressive short-contact regimen (starting at 30 minutes daily, increasing by 30-minute daily) followed by standard overnight application.Baseline demographic and clinical data were recorded, and clinical photographs were obtained. Patients were followed at baseline, 2, 4, and 6 weeks.

The primary outcome measures were changes in comedone count, papule count, and total lesion count. Secondary outcomes included percentage reduction in lesions and assessment of adverse effects such as erythema, dryness, scaling, and burning sensation.

Data were analyzed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation and qualitative variables as frequencies and percentages. Repeated-measures ANOVA and chi-square tests were applied, with $p<0.05$ considered statistically significant.

RESULTS

A total of 40 patients with mild-to-moderate acne vulgaris were included in the study, with 20 patients in each group. Females constituted the majority of patients in both groups. Baseline acne severity was comparable, with most patients presenting with Grade I or Grade II acne.

In the trifarotene group, the mean comedone count decreased from 42.40 ± 21.38 at baseline to 23.35 ± 14.25 at 6 weeks. Similarly, in the adapalene group, the mean comedone count reduced from 26.55 ± 18.50 at baseline to 17.85 ± 15.38 at 6 weeks. The reduction in comedone count was statistically significant in both groups ($p <0.001$). While the trifarotene group presented with a higher baseline lesion load, it demonstrated a higher overall percentage reduction in comedones compared to the adapalene group (44.93% vs 32.77%) over the 6-week period.

Table 1. Comparison of Mean Comedone Count During Follow-up

Follow-up	Trifarotene Mean ± SD	Adapalene Mean ± SD
Baseline	42.40 ± 21.38	26.55 ± 18.50
2 weeks	35.05 ± 18.16	25.25 ± 17.71

4 weeks	28.90 ± 14.85	21.90 ± 16.85
6 weeks	23.35 ± 14.25	17.85 ± 15.38
P value	<0.001	<0.001

Similarly, papule counts showed significant improvement. The mean papule count in the trifarotene group decreased from 8.65 ± 9.86 at baseline to 4.70 ± 5.54 at 6 weeks, whereas the adapalene group showed a reduction from 11.10 ± 5.90 to 7.80 ± 5.49. This improvement was statistically significant in both groups (p<0.001), with superior reduction observed in patients receiving trifarotene.

Table 2. Comparison of Mean Papule Count During Follow-up

Follow-up	Trifarotene Mean ± SD	Adapalene Mean ± SD
Baseline	8.65 ± 9.86	11.10 ± 5.90
2 weeks	7.95 ± 9.34	11.30 ± 6.94
4 weeks	6.35 ± 7.54	10.05 ± 6.21
6 weeks	4.70 ± 5.54	7.80 ± 5.49
P value	<0.001	<0.001

Both groups demonstrated statistically significant reduction in total lesion count over the 6-week follow-up period. Greater reduction was observed in the trifarotene group.

Table 3. Comparison of Total Lesion Count During Follow-up

Follow-up	Trifarotene Mean ± SD	Adapalene Mean ± SD
Baseline	51.05 ± 24.06	37.65 ± 16.27
2 weeks	43.00 ± 20.00	36.55 ± 15.25
4 weeks	35.25 ± 16.64	31.95 ± 15.05
6 weeks	28.05 ± 15.17	25.65 ± 13.18
P value	<0.001	<0.001

Percentage reduction from baseline to 6 weeks was higher in the trifarotene group for all parameters evaluated.

Table 4. Percentage Reduction in Lesion Counts From Baseline to 6 Weeks

Parameter	Trifarotene	Adapalene
Comedones	44.93%	32.77%
Papules	45.66%	29.73%
Total lesion count	45.05%	31.87%

Figure1 Showing Before and After Application Trifarotene for 6 Weeks with 45% of Reduction in Total Lesion Count

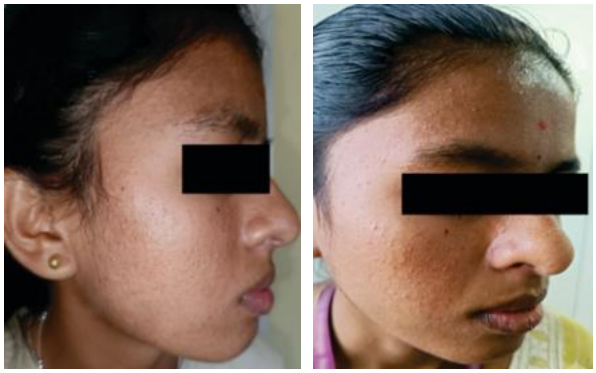

Figure2 Showing Before and After Application Adapalene for 6 Weeks with 31% of Reduction in Total Lesion Count

Both treatment groups showed mild adverse effects, including erythema, dryness, scaling, and burning sensation. Dryness was more commonly observed in the adapalene group. However, there was no statistically significant difference in adverse effects between the two groups (p=0.216).

DISCUSSION

Acne vulgaris is a multifactorial inflammatory disorder of the pilosebaceous unit that significantly affects the quality of life of adolescents and young adults.[1] Topical retinoids remain the cornerstone of acne management because of their ability to normalize follicular keratinization, prevent microcomedone formation, and reduce inflammation.[2] The present study compared the efficacy and safety of topical trifarotene and adapalene in patients with mild-to-moderate acne vulgaris over a six-week period.

Females constituted the majority of participants in both treatment groups, a finding consistent with previous Indian studies that have reported greater healthcare-seeking behavior among female patients.[3] Most participants had Grade I or Grade II acne vulgaris, similar to populations evaluated in earlier studies of topical retinoids.[4]

Both treatment groups demonstrated significant reductions in comedone count, papule count, and total lesion count during follow-up. However, trifarotene showed greater efficacy, producing reductions of 44.93% in comedones, 45.66% in papules, and 45.05% in total lesion count, compared with lower reductions observed with adapalene. These findings suggest superior efficacy of trifarotene in reducing both inflammatory and non-inflammatory acne lesions.

Remarkably, the adapalene group showed a transient increase in mean papule count at week 2 (11.30 ± 6.94 vs 11.10 ± 5.90 at baseline), an initial flare consistent with "retinoid purging." Conversely, the trifarotene group demonstrated progressive lesion reduction from week 2 onward, likely reflecting its targeted receptor selectivity and rapid anti-inflammatory action.

The enhanced therapeutic effect of trifarotene may be attributed to its selective retinoic acid receptor-gamma (RAR-γ) agonistic activity. As RAR-γ is the predominant retinoid receptor subtype in the epidermis, selective targeting may enhance clinical efficacy while limiting off-target effects.[5] Additionally, trifarotene exhibits greater receptor selectivity and rapid hepatic metabolism, thereby reducing systemic exposure.[6] Experimental studies have also demonstrated its potent comedolytic, anti-inflammatory, and depigmenting properties.[7]

The findings of the present study are consistent with phase III clinical trials by Blume-Peytavi et al., which demonstrated significant reductions in inflammatory and non-inflammatory lesions with trifarotene therapy.[8] Similarly, Dréno et al. reported sustained improvement in acne lesions with favorable long-term tolerability.[9] These observations further support the efficacy of trifarotene as a fourth-generation topical retinoid.[10] Although adapalene also produced significant clinical improvement, consistent with previous reports,[11-13] the magnitude of lesion reduction was lower than that achieved with trifarotene.

Adverse effects such as dryness, erythema, scaling, and burning sensation were observed in both groups. Most reactions were mild and transient, and no significant difference in tolerability was noted between the treatments. These findings are comparable with previous studies reporting that topical retinoid-associated irritation is generally self-limiting.[14]

Although the statistical analysis showed no significant difference in overall adverse effects between the two groups (p = 0.216), a higher clinical frequency of mild erythema and scaling was clinically observed in patients treated with trifarotene during the initial two weeks of therapy. This observation aligns with the potent, highly selective epidermal activity of fourth-generation retinoids on the RAR-gamma receptor, which can cause a more pronounced initial retinoid dermatitis before the skin builds tolerance. The lack of statistical significance in these adverse events is likely due to the transient nature of the irritation, which resolved spontaneously by week 4, as well as the study's small sample size.

The present study highlights the potential role of trifarotene as an effective treatment option for mild-to-moderate acne vulgaris in the Indian population.[15] Early and effective treatment is important to prevent long-term sequelae such as scarring and post-inflammatory hyperpigmentation, particularly in darker skin types.[16] However, the

study was limited by its small sample size and short follow-up duration. Additionally, variations in baseline lesion counts between the two randomized groups may serve as a confounding factor; future large-scale studies utilizing baseline-adjusted statistical models (such as ANCOVA) are recommended to further validate these comparative rates of clearance,to evaluate sustained efficacy, relapse rates, and patient-reported outcomes. Overall, topical trifarotene demonstrated superior efficacy to adapalene while maintaining a comparable safety profile.

CONCLUSION

Both topical trifarotene and adapalene were effective and well tolerated in treating mild-to-moderate acne vulgaris. However, trifarotene demonstrated superior efficacy in reducing inflammatory and non-inflammatory lesions, with a safety profile comparable to adapalene. These findings suggest that trifarotene is a promising therapeutic option for acne vulgaris. Further long-term studies are needed to evaluate sustained efficacy and patient outcomes.

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