The Comparative Study to Determine the Efficacy of 0.05% Tazarotene Gel Versus 0.1% Adapalene Gel in Patients of Facial Acne Vulgaris

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Abstract

Introduction: Acne vulgaris is one of the most common skin disorders that present to Dermatology clinics. The majority of the patients suffer from mild-to-moderate acne, for which topical retinoids form the mainstay of treatment. **Aims and Objectives:** The aim of this article is to study and determine the efficacy and tolerability of 0.05% tazarotene gel against 0.1% adapalene gel in facial acne vulgaris. **Materials and Methods:** Eighty-two facial acne vulgaris patients were randomly divided into two groups. Group A was given 0.05% tazarotene gel, and group B received 0.1% adapalene gel to be applied overnight for a period of 8 weeks. Lesion counting and photographs were recorded every 15 days. **Results:** The mean difference on first follow-up from baseline for tazarotene and adapalene was 6.80 ± 6.42 and 1.48 ± 10.44, and the *P*-value was 0.013. The final follow-up visit values were 34.77 ± 23.73 and 25.48 ± 13.04, with a *P*-value of 0.051. The mean percentage change from baseline to last follow-up for tazarotene and adapalene was 60% and 51%, respectively, which were statistically significant for both groups ($P < 0.05$). More patients in the tazarotene group developed cutaneous side effects such as erythema and burning sensation than those in the adapalene group ($P < 0.05$). **conclusion:** About 0.05% tazarotene gel has better efficacy than 0.1% adapalene, though associated with more side effects. It can be used as a topical adjunct or as monotherapy in mild-to-moderate facial acne vulgaris.

Keywords: Adapalene, non-inflammatory acne, tazarotene

Introduction

Acne vulgaris is a common disorder of the pilosebaceous unit seen primarily in adolescents. It is considered to be a multifactorial condition associated with abnormal follicular keratinization, altered sebum production, proliferation of *Cutibacterium acnes*, and altered immune response with inflammation.[1,2] It is also characterized by seborrhea, formation of comedones, erythematous papules, and pustules. Less frequently, nodules, deep pustules, or pseudocysts are also noted which leads to scarring.

It is a physically disabling disease of adolescence and as its prevalence remains high in adulthood, it plays a huge psychological impact contributing to lower self-esteem, anxiety, and depression.[3] Consequently, there is a significant patient-driven demand for effective acne therapies and increased need of topical medications that are popular with patients in order to achieve long-term compliance. As a result, a myriad of agents are available in a variety of formulations.[4]

Differential diagnoses of acne vulgaris are perioral dermatitis, lupus miliaris disseminatus faciei, bacterial folliculitis, miliaria, pseudofolliculitis barbae, rosacea, and seborrheic dermatitis. There are wide array of treatment options available from topical creams to laser devices.

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Retinoids have been found to be very useful in the treatment of acne, especially as they act on both keratinocytes and sebaceous glands. The two important receptors involved are retinoic acid receptors (RARs) and retinoic X receptors, each of which has three subtypes: alpha, beta, and gamma. The gamma receptor is the main mediator of retinoid effects on keratinocytes in human skin.[5]

Tazarotene is a member of acetylenic class of retinoids and chemically it is ethyl 6-nicotinate. It is a retinoid prodrug that is converted to its active form, the cognate carboxylic acid of tazarotene, i.e., tazarotenic acid, by rapid de-esterification in animals and humans. Tazarotenic acid binds to all three members of the RAR family but shows relative selective affinity for RAR-beta and -gamma and may modify gene expression.[6,7]

Adapalene is a naphthoic acid derivative with retinoid receptor agonist properties, which was developed as topical treatment for acne. Adapalene modulates keratinization and possesses anti-inflammatory activities. It selectively interacts with only beta and gamma subtypes of RARs. Selective binding of adapalene to RAR is believed to be the reason for reduced irritation and greater patient acceptability. Adapalene is stable even in the presence of a strong oxidizer (e.g., benzoyl peroxide and light). Adapalene has been demonstrated to penetrate the sebaceous follicles within 5 min of its application onto the skin.[5]

Materials and Methods

This prospective study was conducted at a tertiary hospital after obtaining institutional ethical clearance aiming to assess the efficacy and tolerability of 0.05% tazarotene gel against 0.1% adapalene gel in the treatment of acne.

The sample size for our study was calculated using the following formula:

$$n = \frac{\left\{Z1\sqrt{2P(1-P)} + Z2\sqrt{P1(1-P1) + P2(1-P2)}\right\}^2}{d^2}$$

Source of the formula: Lwanga SK, Lameshow S. Sample Size Determination in Health Studies, 1st ed. Geneva: WHO; 1991.

A sample size of 82 obtained were randomly divided into two groups by using the simple randomization table. Simple clinical grading was used to assign patients with mild-to-moderate facial acne vulgaris.

Mild—Grade I: comedones and few papules;

Moderate—Grade II: comedones, papules, and few pustules;

Severe—Grade III: large inflammatory papules, nodules, pustules, and few cysts;

Very severe—Grade IV: nodules and cysts becoming confluent.

Inclusion criteria were patients with mild-to-moderate acne aged more than 12 years consenting for the study. Pregnant and lactating women, patients with drug-induced acne and cosmetics-induced acne, patients with other skin conditions rather than mild-to-moderate acne, patients with severe nodular acne and clinically infected lesions that require treatment with systemic antibiotics or local antibiotics, patients who had taken topical treatment in the past 14 days and systemic antibiotics in the past 1 month, patients who have taken isotretinoin therapy previously, and patients with a known history of poor drug compliance were excluded. The patients were randomly divided into two groups using the randomization table: group A patients were given 0.05% tazarotene gel and group B were given 0.1% adapalene gel for 2 months.

The detailed history of each patient such as age of onset, prior treatment, family history, and personal history was recorded. Aggravating factors such as seborrhea, photosensitivity, use of cosmetics, seasonal aggravation, use of any oral medication prior to appearance of acne, and history of aggravation with pregnancy and oral contraceptive pills were also recorded. Females were also asked about regularity of menstrual history.

Acne lesions were graded using simple clinical grading. Assessment was done by lesion counting of comedones, and papules (both inflammatory and non-inflammatory) combined for each patient over face were noted at first visit and at subsequent follow-up visits.

Assessment by lesion counting does not provide an objective evaluation but lesion counting is better than grading, because the former distinguishes small differences in therapeutic response. It permits evaluation of effect of treatment on individual lesions and allows examination on acne morphogenesis.[8] The reliability of acne lesion counting is excellent when performed by the same trained rater over time. The high variability between raters appears to be reduced by standardized training.[9]

The Ethical Committee approval was obtained (MGM-ECRHS/2018/35). Photographs were taken at first visit and at every follow-up after written informed consent was obtained from patients and from parents/guardians in case of child participants.

Patients in both groups were instructed to apply the drug once daily overnight as a thin layer over the affected areas and if they develop any irritation after application, they were asked to immediately wash it and gradually increase the application time in the subsequent days. Both groups were adequately informed about the side effect profile of each drug and were strictly instructed to cover the face during sun exposure to avoid photosensitivity. Patients were asked to follow-up every 15 days, and lesion count and any side effects such as erythema, burning, scaling, and flaring of acne lesions were recorded on each visit till 2 months. After 2 months, the treatment was stopped and

patients were asked to come back 1 month later for final follow-up, and the lesion count was recorded 1-month post-treatment along with side effects.

Method of statistical analysis

For analysis, Statistical Package for the Social Sciences (SPSS) 21 software was used. Quantitative data were presented in the form of mean ± SD. For comparison of lesion count between the two groups, the unpaired *t*-test was used; for comparison of difference in the lesion count at each visit from baseline, the paired *t*-test was applied; for comparison of side effects between the two groups, the χ^2 test was applied.

Observations and Results

The mean age group of patients presenting with facial acne vulgaris was 19.5 years, and the most common age group of patients was 16–19 years. Females formed the majority in our study with 51 (62%). Seventy-four (90%) patients seeking treatment were unmarried and nearly 66 (80%) patients of this study comprised students. About half (48%) of the patients had taken topical treatment mostly as "over the counter" for acne previously.

Twenty-one (25%) patients complained of worsening of acne during summer months. Nearly 77 (92%) patients denied use of cosmetics routinely. About 68 (83%) patients complained of persistent seborrhea in their daily life and around 36 (44%) complained of seborrheic capitis. Fifty-one (62%) patients had grade I and 31 (38%) had grade II acne. The average age of onset of acne was 17.3 years, and the most common age group was 15–18 years. These demographic details are tabulated in Table 1.

The mean lesion count on first presentation for tazarotene and adapalene was 57.69 ± 35.88 and 49.88 ± 23.28, respectively. The mean count on fifth follow-up for tazarotene and adapalene was 22.91 ± 15.47 and 24.39 ± 14.35, respectively [Table 2].

The mean difference on first follow-up from baseline was 6.80 ± 6.42 and 1.48 ± 10.44, respectively, and the *P*-value was 0.013 and the final follow-up visit values were 34.77 ± 23.73 and 25.48 ± 13.04 and the *P*-value was 0.051 [Table 3].

Mean percentage changes of total lesions from baseline to final follow-up were 60.28% and 51%, respectively, which were statistically significant for both the groups ($P < 0.05$) [Table 3].

About 94% of the patients of the adapalene group did not develop erythema, whereas only 30% of the patients of the tazarotene group managed to do so, which was statistically significant ($P < 0.001$). Majority of the patients developed scaling in both the groups, which was statistically insignificant. Only 15% of the adapalene

Table 1: Demographic details of patients

Sex distribution (M:F)	31:51
Marital status	90% (unmarried)
Seasonal aggravation	26% (summer)
Occupation	81% (students)
Grade of acne	62% (grade 1)
Age of onset of lesion	44% (15–18 years), 28% (19–22 years)
Age of presentation to clinic	43% (16–19 years), 33% (20–23 years)

It is evident that unmarried teenage students, mainly girls, present to the skin clinic at the earliest

Table 2: Intergroup comparison of the total lesion between the two groups

Lesion	Group 1 Tazarotene	Group 2 Adapalene	*t*-value	*P*-value
	Mean ± SD	Mean ± SD		
Base	57.69 ± 35.88	49.88 ± 23.28	1.0573	0.2943 NS
First follow-up	50.89 ± 31.30	48.39 ± 26.00	0.3560	0.7230 NS
Fifth follow-up	22.91 ± 15.47	24.39 ± 14.35	0.4084	0.6843 NS

P-value: probability value

*Mean lesion count from baseline to final follow-up for tazarotene reduced from 58 to 23 and for adapalene from 50 to 24

Table 3: Intergroup comparison of mean difference and mean percentage change of follow-up from baseline of lesion between the two groups

Lesion	Group 1 Tazarotene	Group 2 Adapalene	*P*-value	Group 1 Tazarotene	*P*-value	Group 2 Adapalene	*P*-value
	Mean ± SD	Mean ± SD		Mean percentage change		Mean percentage change	
First follow-up	6.80 ± 6.42	1.48 ± 10.44	0.0133 Sig.	12%	0.0001 Sig.	3%	0.420 NS
Fifth follow-up	34.77 ± 23.73*	25.48 ± 13.04	0.0515 NS	60%§	0.0001 Sig.	51%	0.0001 Sig.

P-value: probability value; SD: standard deviation

*Mean reduction in lesion count for tazarotene and adapalene after final follow-up compared with baseline was 34.7 ± 23.7 and 25.4 ± 13, respectively

§Mean percentage change from baseline visit to follow-up for tazarotene was 60% and 51%, respectively, which was statistically significant

Table 4: Comparison of side effects between the two groups

Side effects of drugs	Tazarotene	Adapalene
Erythema	24 (71%)	2 (4%)
Scaling	32 (94%)	28 (85%)
Burning	20 (59%)	5 (15%)
Flare	4 (12%)	14 (32%)

Erythema and burning sensation were significantly high in the tazarotene group, whereas flare-up of acne lesions after stoppage of treatment was found to be more with the adapalene group. Scaling was the predominant complaint in both the groups

group patients developed burning sensation compared with 42% in the tazarotene group, which was statistically significant ($P < 0.03$). Flare-up of acne lesions after 2 months of treatment was more with the adapalene group at 43%, whereas it was only 12% for the tazarotene group [Table 4].

Discussion

There are very few studies done to determine the efficacy of 0.05% tazarotene gel in acne vulgaris and even fewer studies that compare it with other retinoids.

In our study, nearly 80% of the patients were students, which was comparable to studies of Adityan and Thappa,[10] who had 66.6% of patients as students. The mean age group of patients presenting with acne was 19.5 years, which was comparable to the study done by Adityan and Thappa, i.e., 19.7 years. The ratio of girls was more compared to boys of 1.6:1, whereas it was 1:1.25 in the study by Adityan and Thappa[10] and 1:1.4 by Sharma *et al.*[11] The mean age of onset of disease in those studies was 15.9 and 14.8 years, respectively. In our study, it was 17.3 years.

The role of cosmetics in aggravation of acne could not be assessed as the majority of patients in our study denied history of using any cosmetics. A study by George and Sridharan[12] in Kerala showed that cosmetics were associated to exacerbation in nearly 40% of population over the age of 25 years. In the same study, they also established that pregnancy had no effect on acne. Our study included only two females with past pregnancy who denied any aggravation of acne. Seasonal variation in our study was observed in 25.2% of the patients which was mainly in summer months, whereas it was 25.9% in a study by Adityan and Thappa.[10] Seborrheic capitis was associated with nearly 43% of patients with acne vulgaris, whereas it was 21.3% in a study by Adityan *et al.*[11,12]

Patients presenting with grade I acne 62% and grade II acne vulgaris 38% were again comparable to the study by Adityan *et al.*, which showed 60.2% with grade 1 acne and 28% had grade II acne.

A study by Amudha *et al.* showed that patients treated with 0.1% adapalene cream showed a reduction rate of 80.3%, and reduction was only 54% in patients treated with 0.1% tazarotene cream at the end of 12 weeks' treatment. Our study showed reduction rates of 61% and 50% for 0.05% tazarotene gel and 0.1% adapalene gel at the end of 8 weeks' treatment, respectively.[13]

An Indian study by Saple *et al.*[14] evaluated the efficacy and safety of tazarotene gel 0.1% in acne vulgaris. In a total of 126 patients tested, the mean reduction in the number of acne lesions was 70.6% in inflammatory and 82% in non-inflammatory acne at the end of 8 weeks' treatment, and it was 86% and 92% at the end of 12 weeks' treatment, respectively. In this study, the side effect profile of tazarotene was very good with only 12% patients experiencing discomfort.

In a recent study by Tanghetti *et al.*,[15] once daily use of tazarotene 0.045% lotion or vehicle in two identical double blind, randomized, vehicle-controlled 12-week studies of acne vulgaris observed a mean percentage change in inflammatory lesions of 55.5% and in non-inflammatory lesions of 51.4% in study 1, whereas the improvement was 59.5% and 60% for inflammatory and non-inflammatory acne in study 2, respectively. Tazarotene 0.045% lotion was well tolerated, and the most common side effects were pain (5%), dryness (4%), and exfoliation (2%).

A double blind randomized trial between 0.1% tazarotene gel and 0.1% tretinoin gel by Leyden *et al.*[16] observed that tazarotene was associated with 60% of reduction in non-inflammatory acne compared with only 38% by tretinoin gel, which were similar to the findings observed in our study.

Another clinical trial by Webster *et al.*,[17] which compared the efficacy of and tolerability of once daily 0.1% tazarotene gel and 0.1% adapalene gel for the treatment of facial acne vulgaris, observed that tazarotene was associated with greater reduction in both inflammatory and non-inflammatory acne (78% vs. 52%), which was statistically significant. Tazarotene patients developed a greater level of burning, pruritus, erythema, and peeling when compared with adapalene ($P < 0.01$) (the proportion of patients in each group who rated the comfort of their treated skin as comfortable or very comfortable was 76% with tazarotene and 69% with adapalene).

A review by Tolaymat *et al.*[18] on adapalene found out that 0.3% adapalene had a greater reduction of acne lesions at 61% compared with 0.1% tazarotene gel at 57%, and adapalene-treated patients experienced less irritation than the tazarotene-treated group.

Our study showed that patients treated with 0.05% tazarotene gel showed improvement by 61% in lesion count after 12 weeks. At weeks 2 and 4, tazarotene gel had a faster onset of action as reductions in acne lesions were 6.8% and 14.3% when compared with patients who used 0.1% adapalene gel, which were 1.48% and 8% reductions in acne

lesion, respectively. The above findings were statistically significant ($P < 0.02$). It can be interpreted that tazarotene has a faster onset of action than adapalene. At the end of 12 weeks, i.e., 4 weeks after treatment, mean reduction in acne for tazarotene was 34.7%, compared with 25.4% of adapalene. This finding was statistically insignificant with *P*-value being 0.051. This can be attributed to flare-up of acne lesions post-treatment for adapalene. Patients with tazarotene experienced more side effects compared with the adapalene group. Erythema was seen in 24 patients of tazarotene, whereas 31 patients did not develop the same, which was statistically significant ($P < 0.0001$).

Burning sensation was not seen in 41% of the tazarotene group and 85% of the adapalene group, which was statistically significant ($P < 0.003$).

Flare-up of acne lesions during and after treatment between the two groups showed that nearly 88% of patients in the tazarotene group and 57% of patients in the adapalene group did not develop it, which was again statistically significant ($P < 0.02$).

Overall, at the end of weeks 8 and 12, improvement in acne lesions for 0.05% tazarotene gel was 49% and 61% when compared with 41% and 50% in the 0.1% adapalene group. The above findings were comparable with many studies by Leyden *et al*. and Webster *et al.*

Limitations in our study were low sample population, lesion count was not taken separately for inflammatory and non-inflammatory lesions, and we could not do long-term follow-up of these patients once they discontinued the treatment. Other scales and quality of life (QoL) were not assessed. The assessment by lesion count does not represent an objective way of the evaluation method.

Conclusion

The growing prevalence of acne in adolescent population is not surprising as many of the students are image conscious in the age of smartphones and social media, change in lifestyle, and early age of puberty. Hence, the need for effective topical drugs at the earliest stage of disease is more.

Tazarotene, a third-generation topical retinoid, has not been studied much on acne patients in India. It reduces both inflammatory and non-inflammatory acne lesions; its efficacy has been shown to be better than adapalene but associated with more cutaneous side effects. Its role in treating acne scars of rolling type is mainly attributed to its irritation potential, which helps in collagen remodeling. Tazarotene can be used as a topical adjunct in moderate-to-severe acne or single drug in mild-to-moderate acne lesions. Adapalene, an undisputed topical retinoid for many decades, is associated with tachyphylaxis and recurrence of acne once stopped.

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Conflicts of interest

There are no conflicts of interest.

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