**ORIGINAL ARTICLE**

# Comparison of Efficacy of 0.1% Tazarotene Versus 0.1% Adapalene for the Treatment of Mild Acne Vulgaris

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## ABSTRACT

**Aim:** To compare the efficacy of 0.1% Tazarotene versus 0.1% Adapalene for the treatment of Mild Acne Vulgaris
**Place and duration of study:** Randomized Controlled Trial was conducted at Dermatology Department DHQ Teaching Hospital, Gujranwala starting from April 2018 to October 2018.
**Methodology:** Data was collected from 120 patients with Grade I and II (Grade I: Comedones, occasional papules and Grade II: Papules, comedones, few pustules). Patients were allocated randomly to group A and group B. Group-A patients were advised to apply Tazarotene while Group-B patients applied Adapalene at night. Response to treatment was evaluated at weeks 4, 8 and 12 by percentage reduction in lesions count at each visit according to scales 0 to 4. A p-value ≤0.05 was considered statistically significant.
**Results:** In Group-A, there were 16(26.7%) males and 44(73.3%) females. While Group-B, consisted of 12(20.0%) males and 48(80.0%) females. The mean age of patients in Group-A was 20.1±4.5 years while in Group-B was 22.1±6.4 years. At week 04, there was a mild improvement in group-A patients and insignificant improvement in Group-B patients. At week 08 Group-A patients showed mild improvement while moderate improvement was seen in Group-B patients. Moderate improvement was seen in group-A patients and marked improvement was observed in Group-B patients at week 12.
**Conclusion:** Tazarotene 0.1% gel is rapidly effective but its side effects make it less suitable a therapy than Adapalene 0.1% gel, so Adapalene gel remains a preferable therapy in desired conditions.
**Keywords:** 0.1% Tazarotene, 0.1% Adapalene, Mild Acne Vulgaris.

## INTRODUCTION

Acne Vulgaris is an extremely serious and recurrent pilosomal inflammatory disease characterised by non-inflammatory (open comedones and near comedones) and inflammatory lesions (papules, pustules, nodules which cysts) and may leave the patient with significant skinscarring.[1] It is the most common dermatological disorder affecting approximately 85 per cent of individuals.[2] Thanks to the early onset of puberty, acne has been seen in younger patients in recent years.[3] Acne is one of the biggest worries amongst young males and females and is associated with psychiatric disturbances e.g. anxiety, depression, loss of thrive, social instability and loss of self-esteem[4].

Management of acne at the earliest period has become a matter of importance. Luckily, with successful treatment, it is possible to improve the quality of life of patients. Wide variety of local and systemic medications have been implemented and a great deal of effort has been placed into reaching consensus on the approach to treatment.

Topical retinoid are the cornerstone of topical acne therapy. These are vitamin A (retinol) or functional analogs with vitamin A activity. They inhibit Toll-like receptor-2, part of innate immune response that triggers inflammation as well. They can reduce proliferation and cohesion of keratinocytes and inflammation as well[5]. The first-generation retinoid (Tretinoin & Isotretinoin) have been widely used for years & now is being replaced gradually by third generation agents like Tazarotene and Adapalene[6,7].

This study focuses mainly on efficacy of topical Tazarotene 0.1% gel and topical Adapalene 0.1% so as to determine an effective modality of treatment for facial acne vulgaris. Adapalene, a synthetic naphthoic derivate, is a third-generation retinoid with anti-inflammatory, comedolytic, and anti-comedogenic properties.[8] It binds selectively to specific nuclear retinoic acid receptors (RARs) and shows greatest affinity for subtypes RARγ, found mainly in the epidermis, and RARβ which is found principally in dermal fibroblasts.[9] It reverses the process of abnormal follicular keratinization thus inhibiting the formation of microcomedo[8].

Moreover, early inflammatory reactions around the pilosebaceous follicle have been shown to be blocked by modulating the expression of TLR2[10]. Adapalene also down-regulates the cell surface receptor used by P. acnes to release pro-inflammatory cytokines[11-12]. This agent is less likely to release pro-inflammatory cytokines.[13] Tazarotene is a new 3rd generation topical acetylenic retinoid and its active metabolite is tazarotenic acid that it can bind all three types of RARs[14]. This normalizes keratinocyte differentiation & filaggrin expression, increases proliferation of keratinocytes, and decreases inflammatory

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marker production. Enhanced esthetic properties can lead to increased compliance with patients.[5,15]

## MATERIALS AND METHODS

This trial was conducted in the Out-patient Department of Dermatology, in DHQ/GMC teaching hospital Gujranwala, during April 2018 to October 2018. Data was collected from 120 patients with Grade I and II (Grade I: Comedones, occasional papules and Grade II: Papules, comedones, few pustules). Acne vulgaris was graded by using a simple grading system that classifies acne vulgaris into four grades[16].

Grade I: Comedones, occasional papules,
Grade II: Papules, comedones, few pustules,
Grade III: Predominately pustules, nodules, abscesses and
Grade IV: Mainly cysts, abscesses, widespread scarring.
All males and females of age >12 years.

Grade-I & Grade-II subjects & patients willing to undergo treatment and follow up, were included. While Pregnant or planning for pregnancy, lactating women, drug induced acneiform lesions, previous isotretenoin usage, estrogens or birth control pills within 90 days of baseline visit, previous systemic antibiotics usage for acne were excluded from study.

Patients were allocated randomly to group A and group B. Group-A patients applied Tazarotene while Group-B patients adapalene once daily in the evening. Base line assessments included age, gender, duration of disease, non-inflammatory lesion count (comedones) and inflammatory lesion count (papules and pustules).

Response to treatment was evaluated at weeks 4, 8 and 12. The efficacy was assessed by percentage reduction in lesion count at each visit according to scales 0 to 4. Completely cleared (100% reduction in lesion count), marked improvement (>75% reduction in lesion count), moderate improvement (50-75% reduction in lesion count), mild improvement (25-50% reduction in lesion count) and Insignificant improvement (<25% reduction in lesion count). Our therapy is defined to be effective if there is >75% reduction in lesions count.

At each follow up patients were asked about side-effects of topical application e.g. irritation, dryness, erythema, pain, photosensitivity (including sunburn), pruritus, any other side effects. Data was analyzed by SPSS v25.0. Qualitative variables were compared by Chi-Square test between groups and continuous variables by t-test between groups. A p-value ≤0.05 was considered statistically significant.

## RESULTS

In Group-A, there were 16(26.7%) were males and 44(73.3%) were females while Group-B included 12(20.0%) males and 48(80.0%) females. The mean age of patients in Group-A was 20.1±4.5 years and in Group-B was 22.1±6.4 years. The mean duration of disease in Group-A was 11.9±11.6 months and in Group-B was 11.3±15.1 months. After 4 weeks, mean improvement was 27.1±20.5% and 25.5±15.3% in group-A and Group-B patients respectively. The mean improvement in Group-A patients after 8 weeks was 43.5±24.9% and Group-B showed 54.1±19.1% improvement. The mean improvement, in Group-A patients after 12 weeks, was 53.1±23.8% and in Group-B, w 80.2±21.1%. Regarding side effects of therapy irritation, dryness, erythema and pruritus was common and seen more with Tazarotene.

Table 1: Comparison of improvement scale after 4 weeks between groups

| **Improvement scale after 4 weeks** | **Groups** | | Total |
|---|---|---|---|
| | **Tazarotene 0.1% gel** | **Adapalene 0.1% gel** | |
| Insignificant (<25% lesion clearance) | 38(63.3%) | 42(70%) | 80(66.7%) |
| Mild (25-50% lesion clearance) | 18(30%) | 18(30%) | 36(30%) |
| Moderate (50-75% lesion clearance) | 4(6.7%) | 0 | 4(33%) |
| Total | 60(100%) | 60(100%) | 120(100%) |

P value 0.350

Table-2: Comparison of improvement scale after 8 weeks between groups

| **Improvement scale after 4 weeks** | **Groups** | | Total |
|---|---|---|---|
| | **Tazarotene 0.1% gel** | **Adapalene 0.1% gel** | |
| Insignificant (<25% lesion clearance) | 22(36.7%) | 6(10%) | 28(23.2%) |
| Mild (25-50% lesion clearance) | 20(33.3%) | 20(33.3%) | 40(33.3) |
| Moderate (50-75% lesion clearance) | 14(23.2%) | 34(56.7%) | 48(40%) |
| Marked (>75% lesion clearance) | 4(6.78%) | 0 | 4(3.3%) |
| Total | 60(100%) | 60(100%) | 120(100%) |

P value 0.013

Table-3: Comparison of improvement scale after 12 weeks between groups

| **Improvement scale after 12 weeks** | **Groups** | | Total |
|---|---|---|---|
| | **Tazarotene 0.1% gel** | **Adapalene 0.1% gel** | |
| Insignificant (<25% lesion clearance) | 8(13.3%) | 2(3.3%) | 20(8.3%) |
| Mild (25-50% lesion clearance) | 28(46.7%) | 4(6.7%) | 32(26.7%) |
| Moderate (50-75% lesion clearance) | 16(26.7%) | 20(33.3%) | 36(30%) |
| Marked (>75% lesion clearance) | 4(6.7%) | 34(56.7%) | 38(31.7%) |
| Complete (100% lesion clearance) | 4(6.7%) | 0 | 4(3.3%) |
| Total | 60(100%) | 60(100%) | 120(100%) |

**P value** 0.00005

Table-4: Comparison of improvemtent after 4, 8 and 12 weeks between groups

| Improvement (%) | Groups | n | Mean | Std. Deviation | p-value |
|---|---|---|---|---|---|
| Improvement after 4 weeks (%) | Tazarotene 0.1% gel | 60 | 27.07 | 20.574 | 0.740 |
| | Adapalene 0.1% gel | 60 | 25.50 | 15.389 | |
| Improvement after 8 weeks (%) | Tazarotene 0.1% gel | 60 | 43.50 | 24.953 | 0.043 |
| | Adapalene 0.1% gel | 60 | 54.00 | 19.182 | |
| Improvement after 12 weeks (%) | Tazarotene 0.1% gel | 60 | 53.13 | 23.840 | 0.00002 |
| | Adapalene 0.1% gel | 60 | 80.27 | 21.092 | |

Table-5: Comparison of adverse effects between groups

| Adverse effects | Groups | | P value |
|---|---|---|---|
| | Tazarotene 0.1% gel | Adapalene 0.1% gel | |
| Irritation | 44(73.3%) | 4(6.7%) | 0.000001 |
| Dryness | 34(56.7%) | 14(23.3%) | 0.008 |
| Erythema | 32(53.3%) | 0 | 0.0002 |
| Pain | 6(10%) | 0 | 0.076 |
| Photosensitivity | 12(20%) | 0 | 0.010 |
| Pruritus | 38(63.3%) | 2(3.3%) | 0.000002 |

## DISCUSSION

One hundred and twency patients with Grade I and II (Grade I: Comedones, occasional papules and Grade II: Papules, comedones, few pustules) attending the Department of Dermatology, DHQ Hospital, Gujranwala, were inducted for the study. Acne involves young adults with almost equal distribution among both the sexes. In a study conducted by smithard et al.[17] 36% were males, but in our study only 23.3% were males. This female preponderance is probably due to the fact that they are more conscious about the acne and seek treatment earlier than males. Mean age of the patients in our study were 21.7 years which is very similar to age distribution as 20.6 years) seen in study done by Webster *et al*.[18]

There have been several comparative studies with different anti-acne topical therapies belonging to retinoids like Tretinoin, Adapalene and Tazarotene. Review of literature showed a single study by Webster et al.[18] wherein efficiency of 0.1% Tazarotene and Adapalene gel have been compared which is similar to our study.

At 4th week, insignificant percentage reduction in lesions count (<25%) on Tazarotene is 38(63.3%) and Adapalene 42(70.0%). Mild percentage reduction in lesions count (25% to 50%) is same in both groups 18(30.0%). Moderate percentage reduction in lesions count (50% to 75%) on Tazarotene is 4(6.7%) with compared to no moderate percentage reduction of lesions count seen in Adapalene group. This shows that Tazarotene 0.1% gel acts faster than 0.1% Adapalene gel as the difference in improvement was statistically insignificant(p=0.350).

Our results were in accordance with studies done by Webster et al.[18] and Leyden et al.[19] wherein the results had proved that Tazarotene 0.1% gel achieves a more rapid rate of clinical improvement than any of the other retinoid including Adapalene.

At 8th week, insignificant percentage reduction in lesions count (<25%) on Tazarotene is 22(36.7%) and in adapalene is 6(10.0%). Mild percentage reduction in lesions count (25% to 50%) is same in both groups that is 20(33.33%). Moderate percentage reduction in lesions count (50% to 75%) on Tazarotene is 14(23.3%) and adapalene is 34(56.7%) that is in favors of or study that adapalene moderately shows its results. However, marked percentage reduction in lesion count (>75%) is noted only 4(6.7%) on Tazarotene group with statistically significant value(p=0.013).

In contrast to our study Bershad S, et al.[20] study outcomes by 12 week shows that Tazarotene shows significantly greater improvement in mean reduction of inflammatory and non-inflammatory lesions with percentage of treatment success (64% and 61% vs 15%; p.001). local adverse effect didn't differ significantly. The results differ as compared to our study, might be due to short contact time of Tazarotene application as in our Tazarotene applied for whole night.

Kakita I et al.[21] study also shows entirely different results as compared to us. He used split face therapy. Both therapies on applied on either side and compared results. Results showed that tolerability of two drugs are same. Reason for good tolerability could be that Tazarotene were applied on alternate day and adapalene daily.

In our study at the end of 12-week treatment period, insignificant percentage reduction in lesions count (<25%) on Tazarotene 8(13.3%) and 2(3.3%) on adapalene. Mild percentage reduction in lesions count (25% to 50%) on Tazarotene 28(46.7%) and 4(6.7%) on adapalene. Moderate percentage reduction in lesions count (50% to 75%) on Tazarotene. is 16(26.7%) and 20(33.3%) on adapalene. Marked percentage reduction in lesions count (75% to 100%) reduction on Tazarotene is 4(6.7%) and 34(56.7%) on adapalene. However, (100%) reduction is seen in Tazarotene group 4(6.7%) only.

This is in partial agreement with the study done by Webster *et al.*[18] Tazarotene 0.1% gel has been found to be superior to Adapalene 0.1% gel with respect to complete clearance of lesions. Our results are supported by Pariser D et al.[22] study that subjects treated with adapalene achieved similar reduction in lesion count at week 12 as compared to Tazarotene; shown to be non-inferior to Tazarotene and during initial stages of treatment, demonstrated better tolerability with respect to erythema and scaling.

Selection of the appropriate treatment depends not only the efficacy but how well the patient can tolerate different formulations.As we consider adverse effects in comparisons, irritation with Tazarotene is 44(73.3%) and 4(6.7%) adapalene with statistically significant value of (p=0.000001). Dryness with Tazarotene is 34(56.7%) and 14(23.3%) adapalene with statistically significant value of

(p=0.008). Erythema with Tazarotene 32(33.3%) as compared to no erythema noted in adapalene group with statistically significant value(p=0.0002). Pain after applying Tazarotene is noted in 6(10.0%) patients compared to painless adapalene application with statistically significant value of (p=0.076). Similar to erythema and pain photosensitivity adverse effect is noted only in Tazarotene group 12(20.0%) patients with statistically significant value of(p=0.010). Pruritus is with Tazarotene is 38(63.3%) and 2(3.3%) adapalene with statistically significant value of(p=0.000002).

Patients encountered untoward symptoms during treatment in previous studies, reported side effects of which 6 (8.96%) had burning, 5 (7.46%) had pruritus, 5 (7.46%) had erythema, 7 (10.44%) had scale and 8 (11.94%) had dry facial skin. Some of the patients had multiple side effects. In our research, the profile of side effects is significantly higher than Saple DG et al.23, Nigam PK et al24 and ASM Zakaria25 reported. These may be due to the drug being used overnight and excessively. The short contact therapy was used by Saple DG et al. and Nigam PK et al. For our show, all the adverse effects are mild to moderate for nature. No drop-out of the study due to adverse events. However, in our study adapalene shows fewer side effects compared to Tazarotene.

Both Tazarotene and adapalene topical agents is better anti-comedogenic and effective in clearance of both non inflammatory and inflammatory lesions but in this study, differences show that Tazarotene 0.1% gel rapidly effective but associated with highly increased levels of burning, peeling and erythema at some point of time than Adapalene 0.1% gel.

## CONCLUSION

Tazarotene 0.1% gel is rapidly effective but its side effects make it less suitable a therapy than Adapalene 0.1% gel, so Adapalene gel remains a preferable therapy in desired conditions.

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