

COMPARISON OF 0.1% ADAPALENE CREAM WITH 0.1% TAZAROTENE CREAM IN THE TREATMENT OF ACNE VULGARIS

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ABSTRACT

BACKGROUND

Acne vulgaris is a self-limiting disorder of the pilosebaceous unit that is seen primarily in adolescents. Acne therapy aims at reduction of sebum production, correcting the abnormal ductal keratinisation, reducing the colony of propionic bacterium acnes and preventing the release of inflammatory mediators that are basically responsible for the pathogenesis of acne.

MATERIALS AND METHODS

The aim of the study was to compare the efficacy of topical adapalene 0.1% cream and topical tazarotene 0.1% cream in the treatment of acne vulgaris. One hundred patients of either sex were enrolled and randomly assigned for the above study. The study was prospective, randomized, single blinded controlled clinical trial. Inclusion Criteria- Patients of either sex with mild to moderate acne vulgaris. Exclusion Criteria- Pregnant and lactating women, age below 12 years and drug induced Acneiform lesions. Number of comedones, papules and pustules were counted and graded. Clinical photographs of the lesions were taken before commencement of therapy and after completion of therapy.

RESULTS

By this study we evaluated the gender and age prevalence, precipitating factors for acne and other associated skin conditions with acne. Treatment with topical adapalene showed good improvement (80.3%) than with topical 0.1% tazarotene cream (54.07%).

CONCLUSION

Patients treated with 0.1% adapalene cream showed excellent response and patients treated with 0.1% tazarotene showed increased side effects and reduced tolerance.

KEYWORDS

Topical Retinoids, Tazarotene Cream, Adapalene Cream, Comedones, Acne Vulgaris.

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BACKGROUND

Acne vulgaris is a self-limiting disorder of the pilosebaceous unit that is seen primarily in adolescents. Most case of acne presents with a pleomorphic array of lesions, consisting of comedones, papules, pustules and nodules with varying extent and severity. While the course of acne may be self-limiting, the sequelae can be lifelong, with pitted or hypertrophic scar formation. The pathogenesis of acne is multifaceted, but four basic steps have been identified. These key elements are: (1) follicular epidermal hyper

proliferation, (2) excess sebum production, (3) inflammation and (4) the presence and activity of propionic bacterium acnes. Each of these processes are under hormonal and immune influence.

Topical retinoids reduce micro comedones and are frequently considered in acne regimens as a means of preventing progression of macrocomedones to active visible lesions. Retinoids reduce abnormal growth and development of keratinocytes within the pilosebaceous duct. It also inhibits the development of the microcomedones and non-inflamed lesions resulting in less anaerobic conditions with few erp. acnes; making the micro environment less favourable for the development to inflammation.^{1,2} Topical retinoids are the main stay of treatment for acne vulgaris as they not only offer efficacy against existing acne lesions, but also help prevent the development of new lesions.³ Adapalene, a naphthoic acid is a synthetic retinoid. Tazarotene is a new generation topical acetylenic retinoid. Both affects cellular

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differentiation, keratinisation and inflammatory process that are abnormally present in acne vulgaris.^{3,4,5}

MATERIALS AND METHODS

The aim of the study is to compare the efficacy of topical adapalene and topical tazarotene in the treatment of acne vulgaris with each other. The agents compared were the following:-

0.1% Adapalene cream.

0.1% Tazarotene Cream.

One hundred patients of either sex were enrolled and randomly assigned for the above study. The study was prospective, randomized, single-blinded, controlled clinical trial. The study was done in the Department of Dermatology, for a period of nine months duration. Inclusion Criteria: Patients of either sex with mild to moderate acne Vulgaris. Exclusion Criteria: Pregnant and Lactating Women, Patients below 12 years of age and drug induced Acnei form lesions.

Patients selected were informed about the nature of study and written consent was obtained from them. The demographic data such as age and sex of the selected patients, occupation, marital status and duration of the disease were taken. Other histories like family history of acne, past and present history of topical and systemic treatments were noted and patients were advised to avoid other treatments for acne. The precipitating factors for acne such as premenstrual flare up, summer exacerbation and stress were noted. History of smoking was also noted. Patients were subjected for general and systemic examination. A thorough dermatological examination was done and other existing dermatological lesions apart from acne were recorded. Number of comedones, papules and pustules were counted and graded. Clinical photographs of the lesions were taken before commencement of the therapy and after completion of the therapy. Patients were instructed to review for every two weeks and report severe side effects immediately, if any. The two commonly used methods of measuring the severity of acne vulgaris are grading and lesion counting. Photography has also been used as a method for measuring the severity of acne.^{6,7,8} 100 patients who fulfilled the inclusion criteria were selected randomly and assigned into two groups. 1st Group is Adapalene 0.1% Cream and the 2nd Group is Tazarotene 0.1% Cream.

Method of Application-The patients were advised to avoid cosmetics and other topical application over the face.

Group – I: 0.1% Adapalene Cream.

Adapalene is applied once a day over the entire face in the evening before retiring to bed. After washing the face, a thin film of the adapalene should be applied, avoiding contact with eyes, lips and mucous membrane.

Group – II: 0.1% Tazarotene Cream.

Tazarotene is applied once a day over the entire face in the evening before retiring to bed. After washing the face a

thin film of the tazarotene should be applied, avoiding contact with eyes, lips and mucous membrane. Tazarotene is initially applied on daily basis and then the application is reduced for alternate days.

For both the groups, the treatment was given for a period of 12 weeks duration. Patients were instructed about the side effects of topical retinoids such as dryness, erythema, skin irritation, skin peeling and itching. Patients were instructed to review for every two weeks and report the severe side effects, if any, immediately. During each visit, the response to the therapy and side effects were noted. Patients were also instructed to avoid sun exposure by using sun protective measures.

Statistical Analysis of the data

The following statistical analyses are used in this study

- Percentage analysis is used to find the exact percentage of respondents
- Mean score was calculated to find the average responses from the respondents..
- Standard deviations were also calculated to find the level of deviations among the respondents.
- One way ANOVA analysis of variance ('f' test) was used to find out the significant difference if any between variables.
- Student 't' test was used to find the significance difference between variables.

This helped in interpretation and interpreted data was summarized.

RESULTS

The following observations were made in the present study and all parameters were tabulated. Of 116 patients 10 patients in the tazarotene group and 6 patients in the adapalene group discontinued therapy prematurely either because of lack of efficacy or adverse events. From the 100 patients 38 patients had Grade I acne and 62 patients had Grade II acne. By this study, the associated skin diseases analysed were seborrheic dermatitis (20%) and Pityriasis versicolor (10%).



Treatment with Tazarotene Cream (0.1%) (Fig. 1)
Treatment with Adapalene Cream (0.1%) (Fig. 2)

Data Analysis

Age	Male		Female	
	Number	Percentage	Number	Percentage
15 to 20	39	60%	20	57%
21 to 25	20	30.7%	13	37%
26 to 29	6	9.2%	2	5.7%
Total	65	100	35	100

Table 1. Cross Tabulation between Age and their Gender

Chi-square test: $\chi^2=2.478$ Df=2 $p>0.05$ Not Significant.

	Average Number of Lesions (weeks)							Average Number of Lesions Reduced	Percentage Reduction
	0	2	4	6	8	10	12		
Comedones	8.2	7.0	6.1	5.0	3.8	2.8	2.2	6.0	73.1%
Papules	5.3	5.0	4.8	3.6	2.2	1.4	0.8	4.5	84.9%
Pustules	1.8	1.0	0.6	0.2	0.0	0.0	0.0	1.8	100%
Total Lesions	15.3	13.0	11.5	8.8	6.0	4.2	3.0	12.3	80.3%

Table 2. Observation of Responses with Topical Adapalene in Group I Patients with Acne (N-50)

One-way ANOVA F' test: $f=21.843$ $p<0.05$ Significant.

	Average Number of Lesions (Weeks)							Average Number of Lesions Reduced	Percentage Reduction
	0	2	4	6	8	10	12		
Comedones	8.4	8.0	7.6	6.4	5.8	5.0	4.1	4.3	51.1
Papules	4.6	4.0	4.0	3.6	3.4	3.3	2.1	2.5	50.40
Pustules	0.5	0.5	0.5	0	0	0	0	0.5	100.00
Total Lesions	13.5	12.5	12.1	10.0	9.2	8.3	6.2	7.3	54.07

Table 3. Observation of Responses with Topical Tazarotene (1% Cream) in Group I Patients with Acne (N-50)

One-way ANOVA F' test: $f=29.182$ $p<0.05$ Significant.

Chi-square test: $\chi^2=11.947$ Df=3 $p<0.05$ Significant.

Side Effects	Group – I Adapalene 0.1%	Group – II Tazarotene 0.1%
Erythema	10	14
Skin Irritation	10	15
Peeling	5	5
Dryness	2	20
Existing Skin Lesions Increased	2	6
Itching	10	8
Infections	-	-

Table 4. Side Effects Observed During Therapy

Chi-square test: $\chi^2=3.874$ Df=6 $p>0.05$ Not Significant

The response following the therapy for both Group I & II
 Nil : 0 to 25% reduction of acne lesions.
 Mild : 26 to 50% reduction of acne lesions.
 Moderate : 51 to 75% reduction of acne lesions.
 Good : 76 to 100% reduction of acne lesions.

Response	Adapalene 0.1% Cream	Tazarotene 0.1% Cream
Nil	-	3
Mild	12	34
Moderate	22	8
Good	16	5

Table 5. The Response Following the Therapy for both Group I & II

DISCUSSION

According to this study the prevalence of acne among the students was 48%. There was a significantly higher rate of acne among male students than that among females. The common age groups affected were between 15-20 years. Our study gave evidence that acne prevalence significantly increased during summer, emotional stress and premenstrual period. History of smoking was obtained from 20% of male patients. In this study family history of acne was observed among 41% of patients. Regarding diet pattern history of taking skim milk was noted in 30% of patients. Most of the findings of this study are found to be similar to that of the study done at South India.

Epidemiological studies have demonstrated that acne is most common in post pubescent teens, with boys most frequently affected.⁹ In another study about one third of patients reported an aggravation of their acne in winter but also approximately one third of the patients complained about an aggravation of their acne in summer.¹⁰

A study suggests a significant association between stress and severity of acne, especially in males.¹¹ Previous studies also concluded that almost half of all women experience premenstrual flares of their acne.¹² A statistically significant difference was noticed for the prevalence acne among the smokers (41.5%) and the non-smokers (9.7%). Deficiency of antioxidants caused by smoking which lead to alterations in sebum composition.¹³ According to prospective cohort study, there is positive

association between intake of skim milk and acne. This finding suggests that skim milk contains hormonal factors that influence endogenous hormones.¹⁴

Group – I

Patients in this group showed a moderate to good response and there was greater reduction of inflammatory and non-inflammatory acne lesions. At the end of 4 weeks, there was 25% reduction of acne lesions and at the end of 8 weeks, the reduction rate was 60%. At the end of 12 weeks of treatment, there was moderate to good response, and the reduction at that time was 80.3%. The side effects such as irritation, itching, dryness, erythema, skin peeling were seen among few patients. The side effects were very minimal and transient compared to topical 0.1% tazarotene cream. During treatment with topical 0.1% adapalene cream patient compliance and overall outcomes were good. Patients showed up for regular and proper treatment. The side effects were observed among few patients only. Most of the patients had no side effects.

GROUP – II

Patients in this group showed a mild response in both inflammatory and non-inflammatory lesions. The side effects were very severe in this study. Most of the patients developed severe erythema, scaling, dryness during the 1st week of therapy. Even though the side effects were transient, the duration of these effects were prolonged and severe compared to topical adapalene. For that reason tazarotene is applied only half as frequently as adapalene. At the end of 4 weeks of treatment, the reduction rate was 7%. At the end of 12 weeks, the overall reduction was 50.04%. Overall, there is moderate to good improvement in the acne lesions with topical 0.1% adapalene cream. Topical treatment with 0.1% tazarotene showed mild improvement with more side effects.

In Clinical trials, 0.1% adapalene has proved to be effective for acne vulgaris. Adapalene has a rapid onset of action and a particularly favourable tolerability profile compared with other retinoids. These attributes can potentially promote patient compliance, an important factor in treatment success.¹⁵ One study showed the mean 21 day Cumulative irritancy indices for adapalene 0.1% cream and gel were significantly lower than those for tazarotene 0.05% and 0.1% creams.¹⁶ According to another study topical tazarotene was effective and well tolerated, regardless of patients acne severity, skin type, sex or ethnicity.¹⁷ One more study also supporting the above statement, by denoting that topical tazarotene cream 0.1% is a effective and safe treatment option for acne vulgaris affecting face. It is mostly effective in grade 1 & grade 2 acne.¹⁸ The above finding regarding topical tazarotene is not correlating with our present study.

According to a study adapalene gel was associated with fewer treatment related adverse events than tazarotene cream (36% Vs 58% respectively) and less than half as many adverse events that were definitely related to study treatment than tazarotene cream (20% Vs 45%

respectively). The findings of this study correlates with the findings of our study.¹⁹ A twelve-week, multicenter, randomized, double blind study concluded that, adapalene cream 0.1% demonstrates superior efficacy and also has excellent tolerability and is associated with a low incidence of cutaneous adverse events.²⁰

According to a study tazarotene was associated with a significantly greater incidence of patients achieving 50% or greater global improvement (77% vs 55% $P < 0.1$) compared with adapalene.²¹ But in our study adapalene was associated with a significantly greater incidence of patients achieving 50% or greater improvement compared with tazarotene. According to a study, preliminary results from the tazarotene Vs adapalene trial suggests that, when tazarotene is applied only half as frequently as adapalene, the two drugs achieved comparable reduction in non-inflammatory and inflammatory lesion counts.²²

A recent multicentre study suggests that tazarotene may be superior to adapalene for reducing comedones. An impressive 77% of the tazarotene treated patients achieved at least a 50% global improvement in acne, compare with 55% of adapalene treated patients who achieved 50% improvement.²³ In one study with overnight topical tazarotene therapy, 9% of patients withdrew due to local irritation. In another study, untoward effects were experienced by 11.9% of patients during the treatment.^{24,19} Other studies also concluded that, topical tazarotene appears to be a safe and effective topical remedy for acne vulgaris.^{25,26}

According to this study, of the patients treated with 0.1% adapalene cream, 12% of the patients showed mild response, 22% with moderate response and 16% showed good response. By this study, of the patients treated with 0.1% topical tazarotene cream, 34% of the patients showed mild response, 8% with moderate response and 5% showed good response.

CONCLUSION

Patients treated with 0.1% adapalene cream showed excellent response compared to patients treated with 0.1% tazarotene cream. The side effects of topical adapalene cream were very minimal compared to topical tazarotene cream, which can improve patient's compliance and overall outcomes. The side effects observed during topical tazarotene cream were very high and patients showed reduced tolerance. The side effects of both drugs were transient only, but compared to topical adapalene cream, topical tazarotene cream showed prolonged duration of side effects. Most of the patients treated with topical adapalene cream were able to tolerate the overnight application. Patients treated with topical tazarotene cream required short duration therapy.

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