EFFICACY AND SAFETY OF SHORT TERM USE OF 0.1% TAZAROTENE GEL IN THE TREATMENT OF MILD TO MODERATE ACNE VULGARIS: A RANDOMIZED-VEHICLE CONTROLLED TRIAL

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ABSTRACT

Objective: To assess the efficacy and safety of 0.1% tazarotene gel in treatment of mild to moderate acne vulgaris.

Methodology: This randomized controlled trial was conducted in Dermatology unit, MTI Lady Reading Hospital (LRH), Peshawar from June to December 2019. Total 90 patients with mild to moderate acne vulgaris were included in the study. Patients were divided into three groups by lottery method. Group A patients received topical 0.1% tazarotene gel in morning and evening application. Group B patients received topical vehicle (plain gel) in morning and 0.1% tazarotene gel in evening while group C received vehicle (plain gel) in both morning and evening. Data was recorded in pre-designed proforma. The one-way analysis of variance (ANOVA) was used to determine statistical significance.

Results: In group A, 19 patients showed 61-95 % decrease while 11 patients showed complete clearance of lesions after treatment with tazarotene gel for 12 weeks. In group B, 17 patients showed 61-95% decrease, 8 patients showed 41-60% decrease while 5 patients showed complete clearance of acne lesions. In group C, 22 patients showed less than 10% while 8 patients showed 10-20% decrease in the number of lesions. The difference was found significant with p-value of 0.000 between three groups in terms of reduction in the number of lesions at 12 weeks of treatment. Erythema, burning, peeling and itching were the main side effects

Conclusion: Short term topical application of 0.1% tazarotene gel is safe and effective for the treatment of acne vulgaris.

Key Words: Acne vulgaris, Tazarotene gel, Comedonal acne, Papulopustular acne, Nodulocystic acne.

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INTRODUCTION

Acne vulgaris, though considered as a self-limiting condition, is a common inflammatory disease in adolescence. About 90% of adolescents are affected with acne, and in 50% of them, the residual symptoms continue to late adolescnce[1]. At 40 years, 1% of male and 5% of female have remnant disease[2]. A rising trend of acne has been observed in children, perhaps due to earlier onset of puberty[3]. Acne may persist for longer durations and may need prolong treatment. Acne vulgaris has recently been reclassified as chronic illness[4]. Apart from physical aspect, acne has psychological consequences and may cause permanent scarring[5]. Therefore patients are more keen to seek early treatment[6].

Morphology and extent of the disease plays important role in treatment[7]. The important progress in management is optimal use of topical retinoids[8]. Most of the experimental studies recommend topical retinoids[9]. There are various retinoids, which include tretinoin, isotretinoin, adapalene, and tazarotene[10]. They are available in various forms such as cream, gel, liquid, and microsphere. All these have different strengths[11]. Its use is not widespread because of acute dermatological reactions[12]. Different trials have recommended use of adapalene due to its good tolerance, whereas other trials recommend tazarotene as most effective drug with

adverse effect as skin irritation[13,14].

The rationale of this study was to assess efficacy and local skin irritation as side effect, using a short-contact method of applying 0.1% tazarotene gel in patients with mild to moderate facial acne.

METHODOLOGY

This randomized controlled trial was conducted in Dermatology unit, MTI Lady Reading Hospital from June to December 2019. A total of 90 patients with mild to moderate acne vulgaris belonging to age group of 12 to 40 years were enrolled in the study. The patients with severe acne, nodulocystic acne, those taking topical or systemic therapy for acne, pregnant and lactating mothers were excluded from the study. Sample size was calculated by WHO sample size software. It was 87 but to make round figure, 90 patient were included in the study. Approval was taken from the institutional ethics review board. Patients were enrolled by non-probability convenient sampling technique. A written informed consent was taken from patients.

Randomization was done by lottery method and patients were divided into three groups. Group A patients received topical 0.1% tazarotene gel with morning and evening application. Group B patients received topical vehicle gel in morning and 0.1% tazarotene gel in evening while group C received topical vehicle gel in both morning and evening. Patients were given identical jars containing tazrotene and vehicle according to groups for morning and evening use. Both tazrotene and vehicle were colorless and odourless. Patients were instructed in detail about application and amount of gel of about pea-size to be used. The application was left for 2 minutes and each patient was directed to increase the application time by 1 min at interval of 3 days iaccording to tolerability, with up to maximum of 5 minutes. Patients were given written instructions to reduce the contact period up to 30 seconds if local side effects like erythema or burning sensation occur with 30 seconds increments after 3 days, in such cases even up to 5 minute, if patient can tolerate.

Clinical assessment was done at 0,2,4,8 and 12 weeks interval. At each visit, the efficacy of medications was assessed by counting number of facial lesions i.e., inflammatory, non-inflammatory and nodulocystic lesions. The treatment was considered efficacious if the total decrease in the number of lesions was 50% or more at 12 weeks of therapy.

Patients were also assessed at each visit for the side effects to measure the safety of the therapy. Clinical assessment of side effects including peeling, erythema, dryness, burning, and itching was done and noted. At each visit, patients were also asked about the occurrence and severity of signs and symptoms since the previous visit, even if by the time of the visit these have resolved.

Data was saved in excel sheet and exported to SPSS version 23 for statistical analysis. Participants' demographic characteristics were presented in frequencies, percentages and mean ± SD where applicable. The type and number and the percentage decrease in the number of lesions were calculated at 0, 2, 4, 8 and 12 weeks follow-up. Chi-square test was applied for the categorical variables. ANOVA was employed to find out differences among the groups. Test of significance was two-tailed and p-value of <0.05 was considered significant.

RESULTS

Out of 90 patients, 26 (28.8%) were male. Mean age of patients was 23.44 (SD 4.954) years. The mean age of patients in group A was 25.13 (SD 4.516) years, in group B it was 22.51 (SD 5.303) and in group C, it was 22.67 (SD 4.729) years as shown in table 1.

The total duration of lesions was from 6 months to 3 years in different groups of patients as given in table 2. Maximum number of patients had 26-50 lesions at the time of presentation. Number and types of lesions in patients is shown in table 2.

Maximum decrease in the number of lesions was seen in group A. The relationship was found significant with p-value of 0.000 between patients on treatment in three groups and percentage decrease in the number of lesions at 12 weeks of treatment as shown in table 3.

Thus patients in group A showed maximum efficacy (Table 4).

Regarding the side effects, erythema, burning sensation, peeling, itching and combination of all symptoms is shown in table 5.

DISCUSSION

In comparison with vehicle gel, there was remarkable decrease in the number of lesions in this study. At 12 weeks, the twice a day use of topical 0.1% tazarotene gel, maximum patients showed 61-95% clearance of lesions, with the remaining patients showing complete clearance of the lesions. Thus it was found more efficacious than vehicle.

The female to male ratio in this study was 2.5:1 which was consistent with Bershad et al., in which the female patients outnumbered male patients, with female to male ratio of 1.8:1[16]. This shows that acne is more common in female. In another study, the mean age of patients was 25 years which was again consistent with this study where mean of patients included in the study was 23.44 years[16,17]. Duration of acne has been observed more than 10 years in the study conducted by Bershad et al. This was against the findings in this study, where

Table 1: Demographic characteristics of patients with acne (n=90)

Characteristics		Group A	Group B	Group C	Total
Mean age		25.13 (SD 4.516)	22.53 (SD 5.303)	22.67 (SD 4.729)	23.44 (SD 4.954)
Gender	Male	15	7	4	26 (28.8%)
	Female	15	23	26	64 (71.1%)

Table 2: Characteristics of acne with patients (n=90)

Characteristics		Group A	Group B	Group C	Total
Duration of acne	<6months	6	15	8	29
	>6m-1year	3	10	14	27
	>1-2years	9	1	6	16
	>2-3years	7	3	1	11
	>3years	5	1	1	7
Number of acne lesions at presentation Number of acne lesions at presentation	0-25	8	4	7	19
	26-50	9	17	16	42
	51-75	9	8	6	23
	>75	4	1	1	6
Types of acne lesions	Open comedones	0	1	4	5
	Closed comedones	6	2	4	12
	Open & closed both	12	6	6	24
	Papulopustular	7	11	5	23
	Nodular	5	7	7	19
	combination of all	0	3	4	7

Table 3: Percentage decrease in number of lesions at 12 weeks (n=90)

Percentage decrease in number of lesions at 12 weeks	Groups				P-value
	Group A	Group B	Group C	Total	
<10 %	0	0	22	22	0.000
10-20 %	0	0	8	8	
21-40 %	0	0	0	0	
41-60 %	0	8	0	8	
61-95 %	19	17	0	36	
Completely clear	11	5	0	16	

Table 4: Group wise efficacy to the treatment at 12 weeks

Efficacy	Group A	Group B	Group C	Total
Yes	30 (33.3%)	26 (28.8%)	0	56 (62.2%)
No	0	4 (4.4%)	30 (33.3%)	34 (37.7%)

Table 5: Facial skin signs and symptoms score in patients with acne after 12 week of treatment (n=90)

Facial skin signs and symptoms	Group A	Group B	Group C	Total
Erythema	13	3	11	27
Burning	8	10	8	26
Peeling	3	13	6	22
Itching	2	2	3	7
Combination of all	1	2	2	5
None	3	0	0	3

the duration of acne was less than 6 months in most of the patients with the least number of patients having acne for more than 3 years[17].

Regarding efficacy, Shalita et al. showed similar findings with significantly greater reduction of upto 68% in the number of lesions in patients on topical 0.1% tazarotene gel after 12 weeks of treatment[18]. In this study the group on once daily application of topical tazarotene gel showed maximum 17 patients showing 61-95% decrease in the number of lesions. In another study in which efficacy of 0.1% once daily application of tazarotene gel for treatment of acne was compared with other retinoids, there was more than 50% global improvement in the lesions on 67% of the cases. This shows that tazarotene once daily application is more efficacious than once daily application of vehicle gel and other retinoid gel application[19]. Webster et al. also showed that once daily application of 0.1% tazarotene improved more that 50% lesions in 78% of the patients enrolled in the study[20]. A study of alternate day use of topical tazarotene gel showed that there was almost the same efficacy for the treatment of acne after 15 weeks of treatment. There was more than 50% global improvement in the acne lesions in 74% of the cases at the end of treatment[21]. Bershad et al. showed that the patients who were using tazarotene gel twice a day showed maximum improvement in the acne lesions. There was 64% decrease in the number of lesions in group on twice a day application of tazarotene gel, 61% decrease in group on once day application of tazarotene and once a day application of vehicle gel and 15% decrease in group using vehicle gel twice a day[16]. Similarly, in this study, group on twice a day application of tazarotene gel showed 61-95% decrease in acne lesions in 19 patients and complete clearance of lesions in 11 patients. Patients on tazarotene gel once a day and vehicle gel once a day showed that tazarotene gel group had more improvement.

During the treatment, there was remarkable decrease in number of all types of lesions in patients with acne in group on twice daily treatment of tazarotene gel. At presentation, maximum number of patients had both open and closed comedones, followed by papulopustular lesions. Nodular lesions were present in less so. Few of the patients had only open or closed comedones or the combination of all lesions. Bershad et al. showed that the maximum patients had both open and closed comedones which was consistent with this study, but it was found contrary to this study that the least number of patients presented with papulopustular lesions at the time of presentation[16].

Among the signs and symptoms after 12 weeks of treatment, erythema was the most common adverse effect noticed in 27 patients. It was followed by burning sensation in the lesions. Peeling, itching was also present in most of the patients. Only 3 patients had no symptoms at all after treatment. Leyden et al. has shown same results in his study regarding safety of the drug[6].

CONCLUSION

Short contact use of 0.1% tazarotene gel twice daily application regimen is both efficacious and safe for the treatment of acne vulgaris irrespective of type and severity.

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CONTRIBUTORS

MMP conceived the idea, planned the study, drafted initial manuscript and supervised the whole project. IU and HZ helped acquisition and analysis of data, critical revision of the manuscript and bibliography. KK helped in critical revision, statistical analysis and finalization of the manuscript after reviewers' corrections. All authors contributed significantly to the submitted manuscript.