Efficacy and Tolerability of 0.1% Tazarotene Cream and 0.05% Tretinoin Cream in the Treatment of Acne Vulgaris

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Abstract:

Background: Acne vulgaris is a chronic inflammatory disease of the pilosebaceous follicles that is seen primarily in adolescents. **Objective:** To compare the efficacy of 0.1% tazarotene cream and 0.05% tretinoin cream in the treatment of mild to moderate acne vulgaris. **Methods:** A randomized controlled clinical trial was done in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. **Results:** At base line mean number of comedones in group A and group B was 12.77 ± 4.01 and 11.80 ± 3.93 respectively (p=0.350) and at final follow up 4.17 ± 4.02 and 3.47 ± 4.00(p=0.501). At base line mean number of papules in group A and group B was 17.30 ± 10.29 and 18.57 ± 13.88 respectively (p=0. 690) and at final follow up 7.63 ± 8.08 and 7.73 ± 9.98 (p=0. 966). At base line mean number of pustules in group A and group B was 0.50 ± 1.33 and 0.53 ± 1.28 respectively (p=0. 922) and at final follow up 0.07 ± 0.37 and 0.00 (p=0. 326). At baseline mean of total acne score was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B(p=0.934) and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B(p=0.846). At 1st follow up 3.3% of both group got excellent response, at 2nd follow up 13.3% of group A and 30.0% of group B got excellent response, and at final follow up 56.7% of group A and 63.3% of group B achieved excellent response. About 73.33% of tretinoin treated patient and 60% of tazarotene treated did not experience any side effects. **Conclusion:** It can be concluded that 0.1% tazarotene cream and 0.05% tretinoin cream is individually effective and tolerability of 0.1% tazarotene is comparable to 0.05% tretinoin in the treatment of mild to moderate acne vulgaris.

Key words: tazarotene, tretinoin , acne vulgaris.

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Introduction:

Acne vulgaris is a chronic skin disease of the pilosebaceous unit, affecting approximately 80% of young adults and adolescents.[1] Excessive sebum production, combined with abnormal desquamation of follicular epithelium, leads to an accumulation of these materials such that the lumina of sebaceous follicles become distended. This precursor, microscopic stage is known as a microcomedo. In this environment, Propionibacterium acnes proliferate and its production of proinflammatory chemotactic and cytokine factors is responsible for the inflammation of acne.[2]

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One study investigated the initiating events for acne lesions, and found that immune changes and inflammatory responses occur before hyper proliferation of keratinocyte, with a pattern similar to a type IV delayed hypersensitivity response. The immune response is led by CD41 lymphocytes and macrophages.[3] Despite its spontaneous regression in most patients, acne persists in 10% of those patients over the age of 25 years.[4] In addition, 2-7% of acne patients experience considerable scarring. Occurring at a difficult age, in these patients, acne has important medical, psychological, and social effects that can have a severe impact on quality of life, which can be mitigated by effective treatment.[5]

The management of acne can be challenging because of the variability in response to treatment and the need for long-term therapy.[6] Currently, there is a variety of topical and systemic therapies that are recommended for the

treatment of acne, including retinoids, antibiotics, benzoyl peroxide, and hormone therapy. Topical retinoids are integral part of acne therapy and are considered appropriate first-line therapy, either alone or in combination with antimicrobials, for all cases of acne with the exception of the most severe.[7] The abnormal desquamation of follicular epithelium can be normalized by topical tretinoin. This agent decreases the cohesion of corneocytes, minimize microcomedo formation and, in time, decrease both clinical noninflammatory and inflammatory lesions.[8]

The US Food and Drug Administration (FDA) approved tazarotene for the treatment of both facial acne vulgaris and plaque psoriasis in 1997. Although dermatologists are now familiar with using tazarotene to treat psoriasis, many have not yet used tazarotene to treat acne. The most probable reason for this appears to be the perception that tazarotene would not be effective and not be well tolerated on the skin of the face stemming from the fact that tazarotene has been associated with local skin irritation in patients with psoriasis.[9] The newer synthetic retinoid derivatives, tazarotene, have demonstrated effectiveness in the treatment of acne in some study. Nevertheless, contrary to many dermatologists' expectations, tazarotene is actually well tolerated in acne and is clinically comparable to that of tretinoin 0.1% gel, tretinoin 0.025% gel, and adapalene 0.1% gel in some study.[10] Clinical studies have shown that topical tazarotene is efficacious in the treatment of patients with psoriasis, acne vulgaris, and photoaging. [11]

To the best of my knowledge no study exploring the efficacy of topical Tazarotene comparing with topical tretinoin in the treatment of acne vulgaris has yet been conducted in Bangladesh. The current study was aimed to evaluate comparative efficacy as well as tolerability of tretinoin cream 0.05% and tazarotene cream 0.1% in the treatment of mild to moderate acne vulgaris.

Methods:

A prospective, open, randomized controlled clinical trial was done in the department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Dhaka, Bangladesh. The duration of the study was from September 2009 to February 2010. Patients of mild to moderate acne vulgaris attending outpatient department of dermatology, BSMMU, Dhaka were selected by consequitive sampling method by us after considering the inclusion and exclusion criteria of patient selection. According to consensus conference on acne classfication- Presence of comedones without significant inflammation and a few or no papules are included in mild acne and presence of comedones with marked inflammatory papules and pustules are included in moderate acne. Inclusion criterias were age 13 to 40 years of both sexes, patients conformed to the following washout periods: 14 days for topical acne medications, 30 days for systemic antibiotics and 12 weeks for estrogen or birth control pills and 12 months for oral retinoids, and female who agreed to practice appropriate contraceptive measure. Exclusion criteria were known case of topical tazarotene or tretinoin hypersensitivity; history of serious allergic reactions to drug treatment; pregnancy, lactation and/or use of oral contraceptives with a specific anti-androgenic action or any oral contraceptive treatment initiated within 3 months before or during the study and patients suffering from nodulocystic acne.

A total number of 60 patients were primarily selected and they were randomized using computer-generated codes into two groups (group-A and group-B), each of which included 30 patients. Complete history, general physical and dermatological examinations were done for all enrolled patients. For women of reproductive age reproductive history, menstrual history, lactation and pregnancy plan was carefully judged. History and physical findings were recorded in a structured questionnaire. Finally those patients, who matched the inclusion and exclusion criteria according to history, physical examina-

tion and freely gave their informed consent, were selected for the study.

Patients were divided into two groups (Group-A and group-B), group A was treated with 0.05% tretinoin cream and group B with 0.1% Tazarotene cream. Both preparations had to be administered in once-daily regimen on both sides of the face at bedtime, and the duration of the total treatment period was 12 weeks. Unused medication were collected after the last assessment. Patients were clinically assessed monthly for three months. Each time the severity index of the disease were calculated and recorded and clinical photographs were taken. The final clinical assessment was done and the severity index was calculated at the end of the third month. Then the patient was followed up at the second month in the post-treatment period to look for any recurrence.

A four point scale was used to measure the level of response to treatment, if >75% clear- Excellent was response; if 50-75% clear- good response if 25-50% clear fair response; if <25% clear poor response.

All collected data were checked for inconsistencies and improbabilities. Data analysis was performed by Statistical Package for Social Science (SPSS), version-16. Data was edited, coded and entered into the computer. Statistical analyses was done and level of significance was measured by using appropriate procedures like chi square test ($\chi 2$) and unpaired t-test. Level of significance (p value) was set at 0.05 and confidence interval at 95%.

Results:

Mean age of Group A patients was 21.73 ± 4.30 and Group B was 19.70 ± 3.44. 50.0% of group a and 58.3% of Group B was from the age group ≤20 and 50.0% of group A and 33.3% of group B was from the age group of >20. 43.3% of group A and 53.3% of group B was male and 56.7% of group A and 46.7% of group B was female (p=0.438).

Table -I

Distribution of groups by age and sex.(n=60)

Age (in year)	Group A (n=30)	Group B (n=30)	
≤20	15 (50.0)#	20 (58.3)	
>20	15 (50.0)	10 (33.3)	
Total	30 (100.0)	30 (100.0)	
Mean ± SD	21.73 ± 4.30	19.70 ± 3.44	0.48
Sex	Group A	Group B	p value*
Male	13 (43.3)#	16 (53.3)	0.438
Female	17 (56.7)	14 (46.7)	

*unpaired t test was done to measure the level of significance.

Group A - Tretinoin Treated

Group B - Tazarotene Treated

At baseline mean number of comedones in group A and group B was 12.77 ± 4.01 and 11.80 ± 3.93 respectively (p=0.350). At 1st follow up mean number of comedones in group A and group B was 7.80 ± 4.11 and 7.77 ± 4.08 respectively (p=0.975), at 2nd follow up it was 6.10 ± 4.03 and 5.63 ± 4.16 (p=0.661) and at final follow up 4.17 ± 4.02 and 3.47 ± 4.00(p=0.501).

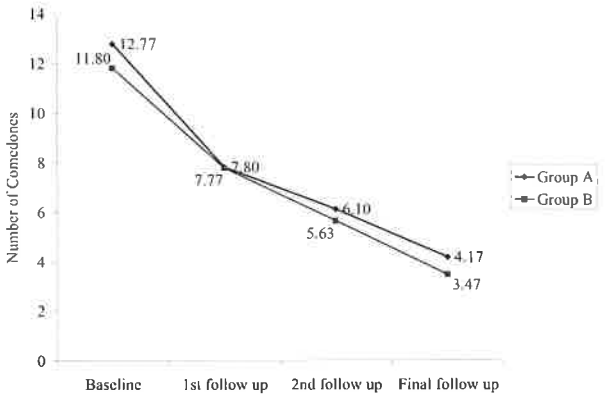

Fig-1: *Line chart of the number of Comedones in different follow up*

At baseline mean number of papules in group A and group

B was 17.30 ± 10.29 and 18.57 ± 13.88 respectively (p=0. 690). At 1st follow up mean number of papules in group A and group B was 12.40 ± 9.4612.40 ± 9.46 and 13.10 ± 12.67 respectively(p=0. 809), at 2nd follow up it was 9.97 ± 8.73and 10.10 ± 11.17 (p=0. 959) and at final follow up 7.63 ± 8.08 and 7.73 ± 9.98 (p=0. 966).

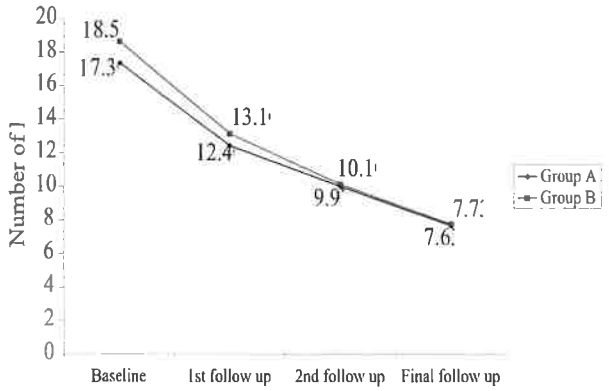

Fig-2: *Line chart of the number of Papules in different follow up*

At baseline mean number of pustules in group A and group B was 0.50 ± 1.33 and 0.53 ± 1.28 respectively (p=0. 922). At 1st follow up mean number of pustules in group A and group B was 0.30 ± 0.88 and 0.30 ± 0.75 respectively(p=0. 999)., at 2nd follow up it was 0.17 ± 0.59 and 0.10 ± 0.31(p=0. 586). and at final follow up 0.07 ± 0.37 and 0.00 (p=0. 326).

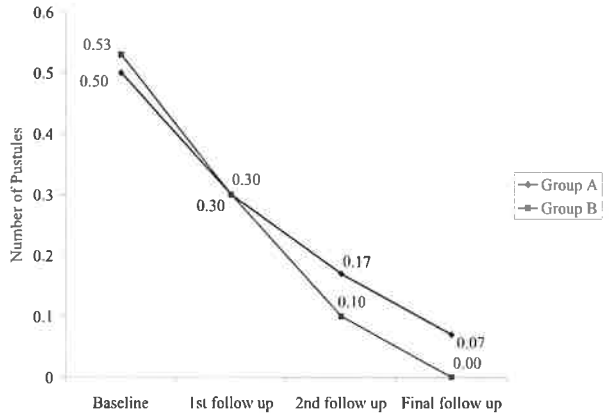

Fig-3: *Line chart of the number of Pustules in different follow up*

At baseline mean of total acne score (acne score of comedones, Papules and pustules) was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B(p=0.934), at 1st follow up it was 20.50 ± 13.64 and 21.17 ± 16.94 respectively in group A and B(p=0.867), at 2nd follow up it was 16.23 ± 12.74 and 15.83 ± 15.29(p=0.913) and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B(p=0.846).

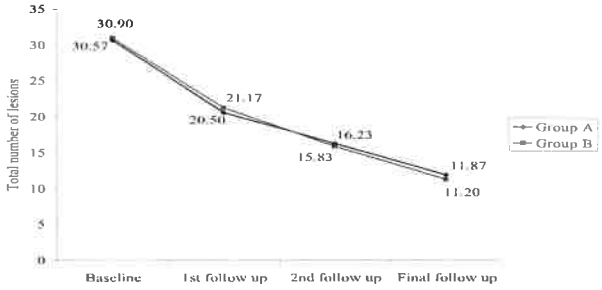

Fig-4: *Line chart of the total acne score in different follow up*

At 1st follow up 3.3% of both group got excellent response, 10.0% of group A and 26.7% group B got good response, 60.0% of group A and 40.0% of group B got fair response and 26.7% of group A and 30.0% of group B got poor response (p=0.317). At 2nd follow up 13.3% of group A and 30.0% of group B got excellent response, 46.7% of group A and 40.0% of group B got good response, 30.0% of group A and 13.3% of group B got fair response and 10.0% of group A and 6.7% of group B got poor response (p=0.470).At final follow up 56.7% of group A and 63.3% of group B achieved excellent response, 13.3% of group A and 16.7% of group B achieved good response, 23.3% of group A and 16.7% of group B achieved fair response and 6.7% of group A and 3.3% of group B achieved poor response (0.828).

Table-II

Distribution of lesions began to clear by groups in different follow up.

Lesions begin to clear	Group Group A	Group Group B	p value*
1st follow up	no %	no%	
•	Excellent	1 (3.3)#	1 (3.3)	0.317
•	Good	3 (10.0)	8 (26.7)	
•	Fair	18 (60.0)	12 (40.0)	
•	Poor	8 (26.7)	9 (30.0)	
2nd follow up			
•	Excellent	4 (13.3)	9 (30.0)	0.470
•	Good	14 (46.7)	12 (40.0)	
•	Fair	9 (30.0)	7 (13.3)	
•	Poor	3 (10.0)	2 (6.7)	
3rd follow up			

•	Excellent	17 (56.7)	19 (63.3)	0.828
•	Good	4 (13.3)	5 (16.7)	
•	Fair	7 (23.3)	5 (16.7)	
•	Poor	2 (6.7)	1 (3.3)	

*Chi square test was done to measure the level of significance
#Figure within parentheses indicates in percentage.

Table-III

Distribution of groups on the basis of side effects.

Safety	Tretinoin group		Tazarotene group	
	N	%	N	%
With side effects	8	26.67%	12	40%
Without side effects	22	73.33%	18	60%
Desquamation	4 (13.3)		3 (10.0)	0.688
Dry skin	2 (6.7)		4 (13.3)	0.389
Burning sensation	1 (3.3)		3 (10.0)	0.301
Irritation	1 (3.3)		1 (3.3)	0.999
Erythema	0 (0.0)		1 (3.3)	0.313

*Chi-square test was done to measure the level of significance.

Side effects recorded in group A were desquamation (13.3%), dry skin (6.7%), burning sensation (3.3%) and irritation (3.3%) and in group B were desquamation (10.0%), dry skin (13.3%), burning sensation (10.0%), irritation (3.3%) and erythema (3.3%) ($p>0.05$).

Discussion:

In present study, mean age of Group A (Tretinoin) was 21.73 ± 4.30 and Group B (Tazarotene) was 19.70 ± 3.44. Different previous studies have reported acne in 28-61% of school children in the age group 10-12 years; 79-95% in the age group 16-18 years; and even in children in the age group 4-7 years.[12,13] In India, prevalence data from a dermatology clinic in a teaching hospital in Varanasi reported acne in 50.6% of boys and 38.13% of girls in the age group 12-17 years.[14] There are believed to be no gender differences in acne prevalence, although such difference are often reported and, very likely, represent social biases.[13] In present study, 43.3% of group A and 53.3% of group B was male and 56.7% of group A and 46.7% of group B was female, with no significant statistical difference ($p>0.05$).

Total acne score was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B respectively at entry level and at the final follow up at the end of the third month it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B ($p>0.05$). In a study by Saple et al, 90.7% and 93.6% of total study cases showed complete to moderate clearance of acne lesions according to physicians at the end of the 8th and 12th weeks of treatment with Tazarotene. There was a statistically significant greater reduction in open comedo count (65 versus 44%) and total noninflammatory lesion count (55 versus 42%) with tazarotene compared with tretinoin.[14] In a similar type of study by Webstster et al, tazarotene had a significantly greater incidence of treatment success and reduction in overall disease severity. In a comparative trial over 12 weeks, once daily application of topical tazarotene 0.1% gel on face seemed to be more efficient in reducing papules and open comedones but similarly effective for closed comedones, than tretinoin 0.05% gel.[15]

In a study by Kakita, the efficacy and tolerability of tazarotene 0.1% gel in the treatment of acne vulgaris have been compared with those of tretinoin 0.025% gel in multicenter, randomized, parallel-group trials. Preliminary results from the tazarotene versus tretinoin trial suggested that once-daily tazarotene is more efficacious than once-daily tretinoin in reducing the numbers of papules and open comedones, and achieves a more rapid reduction in pustules. Both drugs appear to be equally efficacious against closed comedones. The results from the study suggested that the tolerability of tazarotene gel is clinically comparable to that of tretinoin 0.025% gel and tretinoin 0.1% gel.[16]

Kircik et al in a single-center, randomized, parallel design study of the safety and efficacy of tretinoin gel 0.04% to tazarotene cream 0.05% (TAZ) in the management of mild to moderate facial acne vulgaris for 12 weeks proved that efficacy was generally comparable between treatment groups and there was no statistical significance between

the two groups, Tretinoin provided more rapid results in several parameters. Adverse events related to study treatment were rare in both groups and all resolved upon discontinuation of study medication. Compliance has been shown to correlate positively with treatment outcome in acne. [17]

In current study, according to overall global assessment of the disease, at final follow up 56.7% patients of group A (tretinoin) and 63.3% patients of group B (tazarotene) achieved excellent response, 13.3% patients of group A and 16.7% patients of group B achieved good response, 23.3% patients of group A and 16.7% patients of group B achieved fair response and 6.7% patients of group A and 3.3% patients of group B achieved poor response, there was no significant difference between the response of two treatment modalities. So after 12 weeks of the therapy with tazarotene a greater number of patient achieved treatment success compared with tretinoin (80% vs 70%) on the basis of excellent and good response (≥ 50% global improvement) but was not statistically significant ($p > 0.05$). So 0.05% tretinoin and 0.1% tazarotene is effective individually and the efficacy of tazarotene 0.1% is not found superior than 0.05% tretinoin in the treatment of mild to moderate acne vulgaris. And side effects observed were only mild or trace. 73.33% of tretinoin treated patient and 60% of tazarotene treated did not experience any side effects. So both tretinion 0.05% and tazarotene 0.1% is safe individually in the treatment of mild to moderate acne vulgaris.

Conclusion:

It can be concluded that 0.1% tazarotene cream and 0.05% tretinoin cream is individually effective in the treatment of mild to moderate acne vulgaris. And safety & tolerability of 0.1% tazarotene is comparable to 0.05% tretinoin in the treatment of mild to moderate acne vulgaris. Further multicenter, randomized, double-blind study should be conducted with large sample size.

References:

1. Thiboutot D and Gollnick H. New insights into the management of acne: An update from the Global Alliance to Improve Outcomes in Acne Group. J Am Acad Dermatol 2009;60:41-50.
2. Herane MI, Ando I. Acne in infancy and acne genetics. Dermatology 2003; 206:24-28.
3. Jeremy AH, Holland DB, Roberts SG, Thomson KF, Cunliffe WJ. Inflammatory events are involved in acne lesion initiation.J Invest Dermatol 2003;121:20-7
4. Guenther LC. Optimizing Treatment with topical Tazarotene. Am J Clin Dermatol 2003; 4 (3): 197-202
5. Ganceviciene R, Graziene V, Fimmel S. Involvement of the corticotropin-releasing hormone system in the pathogenesis of acne vulgaris. Br J Dermatol. 2008;160(2):345-352.
6. George R, Clarke S, Thiboutot D. Hormonal therapy for acne. Semin Cutan Med Surg. 2008;27(3):188-196.
7. Gibson JR. Rationale for the development of new topical treatments for acne vulgaris. Cutis 1996;57:13-9.
8. Gollnick H, Cunliffe W, Berson D, Dreno B, Finlay A, Leyden JJ, et al. Management of acne: a report from Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol 2003; 49:1-37.
9. Goodman G. Acne and acne scarring – the case for active and early intervention. Aust Fam Physician 2006;35:503–504.
10. Kilkenny M, Merlin K, Plunkett A, Marks R. The prevalence of common skin conditions in Australian school children, III: Acne vulgaris. Br J Dermatol 2005;139:840-5.
11. Lello J, Pearl A, Arroll B, Yallop J, Birchall NM. Prevalence of acne vulgaris in Auckland senior high school students. N Z Med J 2006;108:287-9
12. Bershad S, Singer GK, Parente JE. Successful treatment of acne vulgaris using a new method: results of a randomized vehicle-controlled trial of short-contact therapy with 0.1% tazarotene gel. Arch Dermatol 2002; 138: 481-9
13. Kubba R, Bajaj AK, Thappa DM, Sharma R, Vedamurthy M, Dhar S. Acne in India: Guidelines for management - IAA Consensus Document: Epidemiology of acne. Indian J Dermatol Venereol Leprol 2009;75:63-5.
14. Saple DG, Torsekar RG, Pawanarkar V, Dhanalakshmi UR, Ravichandran G, Kaur D, Dongre N, Desai A. An open study to evaluate the efficacy and safety of tazarotene gel (0.1%) in acne vulgaris. Indian J Dermatol Venereol Leprol 2004;70:92-5
15. Webster GF, Berson D, Stein LF, Fivenson DP, Tanghetti EA, Ling M. Efficacy and tolerability of once-daily tazarotene 0.1% gel versus once-daily tretinoin 0.025% gel in the treatment of facial acne vulgaris: a randomized trial. Cutis.2001; 67:4-9.
16. Kakita L. Tazarotene versus Tretinoin or Adapalene in the treatment of acne vulgaris. J AM Acad Dermatology 2007; 43: 51-4
17. Kircik L. Comparative efficacy and tolerability results of tretinoin microsphere gel pump 0.04% and tazarotene cream 0.05% in the treatment of mild to moderate facial acne vulgaris. J AM Acad Dermatol 2009; 60(3): 14.