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Comparative Safety of 0.1% Tazarotene with 0.05% Tretinoin in the Treatment of Acne Vulgaris

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Summary:

A 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 type acne vulgaris attending outpatient Department of Dermatology (BSMMU), Dhaka were selected by simple random sampling method. A total number of 60 patients were primarily selected and they 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. Mean age of Group A patients was 21.73 ± 4.30 and Group B was 19.70 ± 3.44. 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). At baseline mean of total acne score was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively (p>0.05). 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). But 73.33% of tretinoin treated patient and 60% of tazarotene treated did not experience any side effects. Finally we can conclude that 0.1% tazarotene cream and 0.05% tretinoin cream is individually safe in the treatment of acne vulgaris. And the safety of 0.1% tazarotene cream is comparable with 0.05% tretinion cream in the treatment of mild type of acne vulgaris.

Key words: Safety of 0.1% tazarotene, Safety of 0.05% tretinoin, Acne vulgaris.

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Introduction:

Acne vulgaris is an extremely common disorder affecting up to 95% of the adolescent population and virtually everyone at some point in life. It can lead to significant psychological distress and long-lasting scarring.[1] Acne vulgaris comprises lesions of varying morphology, from comedones, papules, and pustules to nodules and cysts.[2] The pathogenesis of acne is multifactorial. Excessive sebum production, sebaceous follicles with abnormal epithelial hyperkeratinization, the presence of microbial organisms, notably the anaerobic diphtheroid Propionibacterium acnes and inflammation are the key factors involved. [3] The management of acne can be challenging because of the variability in response to treatment and the need for long-term therapy.[4] 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.[1] Topical retinoids are an 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.[4] 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.[5] The newer synthetic retinoid derivative- tazarotene have demonstrated effectiveness in the treatment of acne. But lack of proper research on safety background, many dermatologists' have confusion about tolerance of

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tazarotene in acne.[6] To the best of my knowledge no study exploring the safety 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 safety of tazarotene cream 0.1% and tretinoin cream 0.05% in the treatment of mild acne vulgaris.

Materials and Methods:

A 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 acne vulgaris attending outpatient department of dermatology (BSMMU), Dhaka were selected by simple random sampling method after considering the inclusion and exclusion criteria of patient selection. 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 criterias were skin disorders likely to affect drug absorption or disorders requiring medical treatment within 5 days before the start of the study; 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 moderate or severe type acne or nodulocystic acne.

Ethical issues:

The researcher was duly careful about ethical issues related to this study. In this study the following criteria was set to ensure maintaining the ethical values:

1. All patients were given an explanation of the study including the potential risks and obtainable benefits.
2. All patients were included in the trial after taking their informed consent.
3. The researcher also explained them that they have the right to refuse or accept to participate in the study.
4. All data obtained during study period from the patients remained confidential.

Procedure of data collection:

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

Intervention:

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 and adverse effects were noted at the end of the third month. Then the patient was followed up monthly in the post-treatment period for monitoring of all adverse effects.

Data processing and analysis:

Data were edited, coded and entered into the computer. Statistical analysis was done and level of significance was measured by using appropriate procedures like chi square test ($\div^2$), relative risk (RR) measurement, t-test, and proportion (d) test and others where applicable. 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 d”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). At baseline mean of total acne score

was 30.57 ± 13.62 and 30.90 ± 17.17 in group A and B, at 1st follow up it was 20.50 ± 13.64 and 21.17 ± 16.94 respectively in group A and B, at 2nd follow up it was 16.23 ± 12.74 and 15.83 ± 15.29 and at final follow up it was 11.87 ± 12.04 and 11.20 ± 13.85 respectively in group A and B (p>0.05). Percent reduction of acne severity from base line to final follow up was 69.20 ± 23.41 in group A and 74.77 ± 23.30 in group B (p=0.360). The table II showed that 73.33% of tretinoin treated patient and 60% of tazarotene treated patient did not experience any side effects. 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).

The side effects experienced by patients of different groups in their first follow up were shown in table IV. In 1st follow-up visit, in group A- desquamation, dry skin, burning sensation, irritation and erythema were present in 6.7%, 3.3%, 3.3%, 0% and 3.3% of patients respectively. In group B desquamation, dry skin, burning sensation, irritation and erythema were present in 3.3%, 0%, 3.3%, 3.3%, and 3.3% of patients respectively. In 3rd follow-up visit, in group A- dry skin, burning sensation were present in 3.3% and 3.3% of patients respectively and desquamation, irritation and erythema were absent in group A. In group B dry skin, burning sensation, irritation and erythema were absent and only desquamation was present in 3.3% cases in 3rd follow-up visit.

Table-I

Distribution of age by groups

Age (in year)	Group		p value*
	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		p value*
	Group A	Group B	
Male	13 (43.3)#	16 (53.3)	0.438
Female	17 (56.7)	14 (46.7)	
Total	30 (100.0)	30 (100.0)	

*unpaired t test was done to measure the level of significance
#Figure within parentheses indicates in percentage.
Group A = Tretinoin .05% , Group B = Tazarotene cream (0.1%)

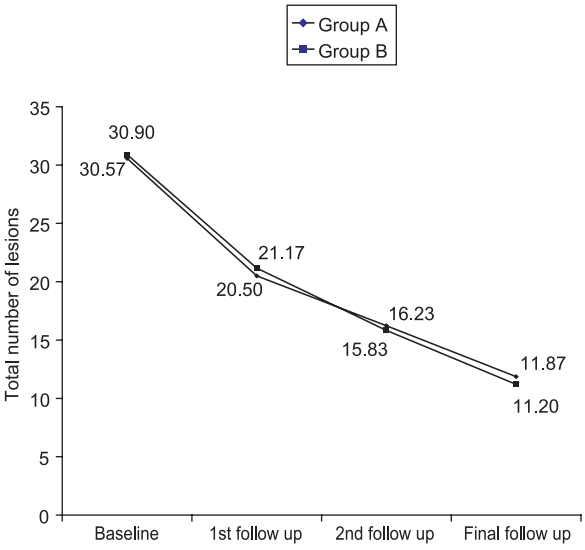

Fig.-1: *Line chart of the total acne score in different follow up*

Table-II

Distribution of side effects observed in the study

Safety	Tretinoin group		Tazarotene group	
	N	%	N	%
With side effects	8	26.67%	12	40%
Without side effects	22	73.33%	18	60%

Table-III

Distribution of side effects by groups

Side effects	Groups		p value*
	Group A	Group B	
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.

Table-IV

Distribution of side effects in 1st follow up and 3rd follow up.

1st follow up	Group A	Group B
Desquamation	2 (6.7%)	1 (3.3%)
Dry skin	1 (3.3%)	0 (0%)
Burning sensation	1 (3.3%)	1 (3.3%)
Irritation	0 (0%)	1 (3.3%)
Erythema	1 (3.3%)	1 (3.3%)
3rd follow up	Group A	Group B
Desquamation	0 (0%)	1 (3.3%)
Dry skin	1 (3.3%)	0 (0%)
Burning sensation	1 (3.3%)	0 (0%)
Irritation	0 (0%)	0 (0%)
Erythema	0 (0%)	0 (0%)

Discussion:

The efficacy of tazarotene in acne is well established. The current study was conducted to evaluate the safety of topical 0.1% tazarotene cream in the treatment of acne vulgaris comparing with topical 0.05% tretinoin gel. Equal of thirty patients of acne vulgaris were treated with topical 0.1% tazarotene cream and 0.05% tretinoin gel. Mean age of Group A (Tretinoin) was 21.73 ± 4.30 and Group B (Tazarotene) was 19.70 ± 3.44, and mean age of acne onset was 19.37 ± 4.07 years and 17.42 ± 3.12 years in group A and group B respectively. 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.[7,8] 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. [9]

There are believed to be no gender differences in acne prevalence, although such difference are often reported and, very likely, represent social biases. [10] 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). Percent reduction of acne severity from base line to final follow up was 69.20 ± 23.41 in tretinoin group and 74.77 ± 23.30 in group tazarotene (p=0.360). Preliminary data from well-controlled clinical trials suggest that the tolerability of tazarotene in the treatment of acne vulgaris appears to be clinically comparable to that of both tretinoin and adapalene. [11]

Side effects were more in tazarotene group than tretinoin group. Side effects recorded in tretinoin treated group were desquamation (13.3% of patietns), dry skin (6.7% of patients), burning sensation (3.3% of patients) and irritation (3.3% of patients). Side effects observed in tazarotene treated group were desquamation (10.0% of patients), dry skin (13.3% of patients), burning sensation (10.0% of patients), irritation (3.3% of patients) and erythema (3.3% of patients). There is no significant difference between two groups (p>0.05). 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 acne vulgaris. And safety & tolerability of 0.1% tazarotene is comparable to 0.05% tretinoin in the treatment of mild acne vulgaris.

Conclusion:

Finally we can conclude that 0.1% tazarotene cream and 0.05% tretinoin cream is individually safe in the treatment of mild acne vulgaris. And the safety of 0.1% tazarotene cream is comparable with 0.05% tretinion cream in the treatment of mild acne vulgaris. Further multicenter, randomized, double-blind, controlled study should be conducted with large sample size, in future.

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