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Research Article

A Comparative Study on Clinical Response of Topical Tazoretene to Topical Corticosteroids in Chronic Plaque Psoriasis

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Abstract: Tazarotene, the first of new generation receptor selective topical retinoid, currently being investigated and widely used in treatment of mild to moderate psoriasis. The objective of the study is to evaluate the safety and efficacy of topical tazarotene gel 0.1% in comparison with corticosteroid mometasone furoate 0.1% cream in treatment of chronic plaque psoriasis. 50 patients of chronic plaque psoriasis enrolled in to the study, were divided into two groups of 25 each randomly. One group received once daily application of tazarotene gel and the other group received mometasone furoate cream once daily. Both the groups received treatment for 12 weeks with evaluation of PASI scores at 0, 8 and 12 weeks. Both tazarotene gel and mometasone cream were significantly effective in reduction of PASI scores both at 8 and 12 weeks of treatment. Mometasone had a greater significant effect than tazarotene in reduction of PASI score and treatment success. Tazarotene was associated with significant reduction in the severity of clinical signs of psoriasis and were found to be safe with acceptable tolerability. Though mometasone furoate was found to be superior to tazarotene, it can still be used in place of corticosteroids for mild to moderate cases to overcome the well known adverse effects of corticosteroids.
Keywords: Tazarotene, Mometasone, Chronic Plaque Psoriasis, Safety, Efficacy.

INTRODUCTION

Psoriasis is a chronic papulosquamous disorder of the skin of unknown etiology. It is characterized by a chronic relapsing nature and variable clinical features [1]. It follows an irregular course characterized by remissions and exacerbations. The disease has a worldwide distribution and affects men and women of all ages, races and social strata [2]. The pathogenesis of psoriasis involves both genetic predisposition including the influence of genes of the human leucocyte antigen complex and T-cell dependent mechanisms [3]. A single lesion may persist for life or many lesions may be present. Some patients are never completely free of the disease whereas others experience long-term remission. When a single disease of unknown etiology has multiple alternative modes of therapy, no one form of therapy is ideal [4]. This is especially true of psoriasis for which multiple alternative treatments are used. Newer aspects of therapies or therapeutic approaches are added frequently. These many forms of therapy all have their own benefits and drawbacks, often no single treatment is ideal and it is rare for a patient not to receive several alternative treatments during his or her life time. The aim of treatment is to produce clearing of the lesion, but the patient sometimes has to settle for a compromise of partial clearing when complete clearing and prolonged remission can be achieved only at the expense of unacceptable treatment toxicity.

The treatment of psoriasis remains a challenging and often a frustrating experience for the doctor. The spectrum of a relapse looms large over the minds of the patient and the doctor. Many factors can influence the choice of therapy for psoriasis. Two major factors influencing choice of psoriasis therapy are the extent or type of the disease and the age of patient [4, 5]. In general, the simpler and potentially less toxic therapies should be tried first, including phototherapy with tar and ultraviolet B radiation. Other local therapies are Dithranol (Anthraline), corticosteroids, salicylic acid, calcipotriol, vitamin D3 analogue, arachidonic acid, topical methotrexate, topical retinoids, topical cyclosporine and capsaicin [1, 6]. In case of severe form of disease and relapse systemic drugs like corticosteroids, methotrexate, hydroxyurea, retinoids, etretinate, isotretinoin, cyclosporine A etc are used. The goal of treatment should not necessarily be total clearing, but achievement of adequate control at the lowest possible drug dosage and side effects. Various forms of treatment have been developed in the past several decades. They have all been developed empirically, as the disease is of unknown cause new drugs and regimens are constantly being tried out.

Among such new advances are the third generation retinoids such as tazarotene and adapalene, which are currently being investigated [7]. Tazarotene is the first of new generation receptor selective topical retinoids with selective activity in skin in psoriasis with limited undesirable effects at receptor level [8]. It is also claimed to have a prolonged remission free period after treatment. So the need for the study is to compare the clinical response of topical tazarotene to well established corticosteroids

MATERIALS AND METHODS

To evaluate the efficacy of topical tazarotene gel 0.1% in comparison with corticosteroid mometasone furoate 0.1% cream in treatment of chronic plaque psoriasis. The study was conducted on fifty patients of chronic plaque psoriasis.

Inclusion criteria

Adult patients with clinically confirmed diagnosis of chronic plaque psoriasis. Both sexes were included with less than thirty percent of psoriasis.

Exclusion criteria

Children less than 12 years of age, pregnant women, lactating mother, women of child bearing age group not on ontraceptives, evidence of hepatic or renal impairment and other skin infections which can be misleading.

History and clinical examination

Initially name, age, sex, occupation and full address were recorded. A written informed consent was taken from all patients. A detailed history of present illness like age on onset, duration of illness, site of onset, past modality of treatment, seasonal variations, aggravating factors, family history of psoriasis and other associated systemic diseases present were noted [9].

General examination and grading

A complete general physical examination, systemic examination and local examination of skin were done. Skin examination was done in detail with special reference to the morphology of lesions like erythema or redness, duration or thickening, extent of scaling and the extent of skin involvement. A fresh lesion was scraped with a clean sterile glass slide to find out the type of scaling and to look for Auspitz's sign. Nails, mucous membrane and joints were examined for involvement of psoriasis.

Psoriasis Area and Severity Index (PASI)

The assessment of the effectiveness of new treatment for soriasis is limited by the lack of any objective measure of disease severity [10]. Though psoriasis area and severity index (PASI) has limitations, it remains the gold standard, a fossil tool of medical assessment [11]. The PASI score is calculated as follows [12]:

$$PASI = 0.2 (EU+SU+IU) AU+0.3 (ET+ST+IT) AT+0.4 (EL+SL+IL) AL$$

Where;

E = Erythema or redness U = Upper limb
I = Induration T = Trunk
S = Scaling L = lower limb
A = Area of involvement

Area of extent of lesion is classified on a 7-point scale as

0 – No involvement
1 – Less than 10% 64
2 – 10-29%
3 – 30-49%
4 – 50-69%
5 – 70-89%
6 – 90-100%

The severities of lesion (erythema, scaling, induration) are classified on a 5-point scale.

0 – Complete lack of involvement
1 – Mild involvement
2 – Moderate involvement
3 – Severe involvement
4 – Severest possible involvement

After selecting the patients based on inclusion and exclusion criteria, with signed consent fifty patients of chronic plaque psoriasis were included in to the study. The patients were randomly divided in two groups of twenty-five each. Group I consisting of twenty-five patients was allotted to tazarotene group. The group II of twenty-five patients was allotted to corticosteroid group. The study was conducted over a period of three months.

Medication

Group I: Topical tazarotene strength 0.1 % once daily application thinly and evenly, in the evening. They were advised to avoid excessive sun exposure.

Group II: Topical mometasone – furoate strength 0.1% once daily in the morning [13]. Liquid paraffin was also advised for local application for prevention of dry skin.

Each patient underwent baseline hematological investigations for Hb%, total blood count, differential count, ESR and biochemical tests like serum proteins, serum creatinine, serum alkaline phosphatase, blood urea and serum bilirubin. The patients also underwent baseline psoriasis area and severity index (PASI) estimation and recorded in proforma.

Follow-up

The patients were called back for follow up at 8 weeks and at 12 week of completion of treatment in both the groups. The follow up included the following.

- Improvement in signs and symptoms was graded using the PASI scale.

- Any adverse effects due to the medication were noted and treated.

Statistical Analysis

Descriptive data were expressed as mean ± standard deviation. Continuous data post treatment changes compared to baseline was analyzed by paired Student t-test and inter group by unpaired t-test. Where data may not have been normally distributed (PASI score) non-parametric test (intra-Wilcoxon rank score test, inter-Mann-Whitney test) were used. Categorical data was analyzed by Chi-square test. For the entire test a p-value of 0.05 or less was considered for statistical significance.

RESULTS

Table 1: Age and sex distribution

Age(yrs)	Group 1			Group II			Male		Female		Total	
	Male	Female	Total	Male	Female	Total	No.	%	No.	%	No.	%
	No.	No.		No.	No.							
≤20	1	0	1	0	0	0	1	2.70	0	0	1	2
21-30	6	3	9	6	3	9	12	32.42	6	46.15	18	36
31-40	4	0	4	7	2	9	11	29.72	2	15.38	13	26
41-50	4	1	5	3	1	4	7	18.91	2	15.38	9	18
51-60	2	2	4	3	0	3	5	13.51	2	15.38	7	14
≥61	1	1	2	0	0	0	1	2.70	1	7.69	2	4
Total	18	7	25	19	6	25	37	100	13	100	50	100
Mean±SD	41.0±14.8			37.6±9.2			39.16±11.4		39.76±15.29		39.32±12.3	
Range	16-75			26-57			16-70		24-75		16-75	

In the present study majority of the patients belonged to the age group of 21 to 30 years [in group 1(tazarotene) 36% and group 2 (mometasone) 36%]. The overall study showed majority of patients belonged to age group of 21 to 30 years (36%) followed by the age group 31-40 years (26%).thus most of the patients (62%) belonged to age group of 21 to 40 years.

The incidence was lower below the age of 20 years and above the age of 60 years. The youngest person in the study was 16 yrs and oldest 75 yrs. the overall mean age distribution was 39.32 yrs, 39.1 in males and 39.7 in females.

Table 2: Duration of disease

Duration (yrs)	Group 1		Group II		Total	
	No.	%	No.	%	No.	%
<1	1	4	1	4	2	4
1-6	19	76	18	72	37	74
7-12	5	20	4	16	9	18
>12	0	0	2	8	2	4
Total	25	100	25	100	50	100
Mean±SD	4.06±3.0		5.06±4.0		4.56±3.55	
Range	5 months -12 yrs		7 months -16 years		5 months -16 yrs	

In the present study the mean duration of disease in the group 1 was 4 yrs and group 2, 5 yrs. The overall duration was 4.5 yrs .74% of the patients had the disease for longer than 1 year, of whom 22 % had the duration of more than 7 yrs. 4% of patients had duration less than one year.

Table 3: Family history

Family history	Group 1		Group II		Total	
	No.	%	No.	%	No.	%
Present	1	4	3	12	4	8
Absent	24	96	22	88	46	92
Total	25	100	25	100	50	100

In the present study one patient had a family history of psoriasis in group1 and 3 patients in group 2.in the overall study 8% had family history and the majority 92% had no family history prior.

Table 4: Associated conditions and aggravating factors

Variants	Group 1		Group II		Total	
	No.	%	No.	%	No.	%
Associated conditions						
Diabetes mellitus	2	8	2	8	4	8
Hypertension	3	12	4	16	7	14
Aggravating factors	8	32	7	28	15	30

In the present study diabetes was seen in 8% of the patients in both the groups.hypertension in 12% of the group 1 and 16% of the group 2.the overall diabetes was 8% and hypertension 14%.the most common aggravating factor in both the groupwas stress, 32% in group 1 and 28% in group 2 .the overall percentage of stress in the study was 30%.

Table 5: Pre-treatment clinical variables of patients

Variables	Group 1	Group II	t/Chi	p-value
Age (years) ± SD	41±14.8	37.6±9.2	0.99	0.33,NS
Age of onset (yrs) ±SD	36.76±	32.56±	1.33	0.19,NS
Duration of Disease±SD	4.06±	5.06±	1.01	0.32,NS
Females (%)	28	24	p=0.75,NS	
Males (%)	72	76		
Baseline PASI (±SD)	8.8±2.5	10.4±2.6	2.19	0.03,S

In the present study all pretreatment clinical variables like age, age of onset, duration of disease and sex ratio showed no significant difference (p>0.05). The baseline PASI score was higher in group 2 compared to group 1.

Table 6: Changes in PASI scores (Mean ± SD)

Groups	Particulars	Base line	8 wks	Diff	% diff	12 wks	Diff	% diff
Group-I	Mean	8.8	8.2	0.6	5.3	4.6	4.1	47.3
	±SD	2.5	2.4	1.1	10.0	1.8	1.6	11.6
	Z*	-	-	3.28	-	-	4.37	-
	p-value	-	-	p<0.01,S	-	-	p<0.001,HS	-
Group-II	Mean	10.4	8.9	1.5	13.4	3.3	7.0	68.0
	±SD	2.6	2.2	1.4	11.2	1.5	2.3	13.8
	Z*			3.72	-	-	4.37	-
	p-value	-	-	p<0.01,S	-	-	p<0.001,HS	-
I Vs II	Mean Diff			0.9	8.1	-	2.9	20.7
	p-value			<0.001HS			p<0.001,HS	

Group 1(tazoretene): The reduction or difference of mean PASI score both at 8 weeks and 12 weeks post treatment compared to baseline was found to be statistically significant (p<0.01 at 8 weeks, p<0.001 at 12 weeks).

Group 2 (mometasone) the reduction or difference of the mean PASI score both at 8 weeks and 12 weeks post treatment compared to baseline was found to be statistically highly significant (p<0.001).

Group 1 vs group 2: On comparing both groups, there was a significant difference between mometasone and tazarotene group which was in favor of mometasone both at 8 weeks and at 12 weeks of the treatment (p<0.001).the mean difference from baseline was more in mometasone group both in 8 and 12 weeks compared to tazoretene.

Table 7: Global Response in PASI

Groups	Percentage of cases showing clearance						Total (%)
	100%	<100to ≥90	<90 to ≥75	<75 to≥50	<50to ≥25	<25%	
I	0	0	0	52	48	0	100
II	4	4	16	68	8	0	100

In the present study in Group I 52% of patients showed improvement or clearance between 50 to 75% and 48% of patients showed clearance between 25 to 50%. In group II, 4% showed 100% clearance, 4% showed a clearance of 100 to 90%, 16% clearance of 90 to 75% and 68% clearance of 50 to 75%. Treatment

success was defined as a good or excellent response on improvement of 50% or more [14]. The tazarotene group showed 52% and mometasone group 68% in the treatment success. Thus both groups showed a success rate of more than 50%.

Table 8: Adverse effects

Adverse effects	Group 1		Group II		Total	
	No.	%	No.	%	No.	%
Burning sensation	5	20	-	-	8	16
Hypopigmentation	-	-	2	8		
Striae	-	-	1	4		
Total	25	100	25	100	50	100

The most common adverse reaction in group I was mild to moderate burning sensation in the lesions (20%) and in group II the adverse reaction seen in the study were hypopigmentation (8%) and striae (4%). The overall adverse reactions in the study was 16% of patients.

DISCUSSION

Age Distribution

In the present study 18 (36%) patients belonged to age group of 21 to 30 years followed by 13 (26%) patients to age group of 31 to 40 years. Thus the majority of patients (62%) belonged to the age group of 21to 40 years. The incidence of psoriasis in age group of less than 20 years was 2%, and in the age group of above 50 years was 36% of total cases. The average age of patients in the present study was 39.32 years, females 39.76 years and males 39.16 years. Zrnic *et al*. [15] reported the average age of psoriatic patients was 37.33 years, 35.55 years in females and 38.20 years in males. Sharma and Sepaha [16] had revealed that psoriasis was commonest (76.6%) in the middle age groups between 15 to 45 years, maximum being in 15 to 30 years age period. The incidence was much lower above the age of 45 years (16.67%) and below the age of 15 years (6.66%). Thus the results of present study are similar to above mentioned.

Duration of disease

In the present study 4% of patients had the disease for less than 1 year and 96% had duration for more than one year, of whom 22% had the disease with remissions and exacerbations for more than 7 years. The majority of patients (74%) were between 1 to 6 years. The mean duration of disease was 4.56 years with range from 5 months to 16 years. Sharma and Speaha16 reported 83.33% of patients having duration of above one year. Ambadi *et al*. [17] reported 31% patients having duration of psoriasis below 1 year and 68.9% patients having duration above 1 year. Mean duration was 3.1 years with a range from 2 months to 12 years.

The findings in present study are comparable with the study of Sharma et al. In comparison with Ambadi *et al*. [17] the percentage of patients below one year was less probably because of lack of awareness regarding the disease and ignorance to come forward for treatment of disease. The prolonged duration of disease reveals the chronic nature of the disease.

Family History

In the present study 8% (4) of patients had a family history of psoriasis. Inderjeet Kaur *et al*. [18] reported a family history of 7%. Gunawardene *et al*. [19] reported a family history of 8.3%. Zrnic *et al*. [15] reported a family history of 8.5%. Thus the family history in the present study is within the range observed in the above studies. This indicates the possible role of genetic factors in etiology.

Associated Conditions and Aggravating Factors

In the present study 30% of patients attributed the initiation or worsening of their disease to stress. Farber *et al*. [20] reported stress in 23 to 42% of their patients. Farber *et al*. [21] reported that in 32 to 44% of their patients, stress contributed for the appearance or worsening of their lesions. Thus the finding in the present study are in concurrence with the above studies [22]. In the present study there was incidence of diabetes mellitus in 8% and hypertension in 14% of patients.

Pretreatment Clinical Variables of Patients

The pretreatment clinical variables of patients in both the treatment groups were compared and analyzed. All variables like age of patients, age of onset, duration of disease and sex ratio in both groups showed no significant difference. The baseline PASI score was slightly on higher side in the mometasone groups (10.4) compared to tazarotene group (8.8). The two treatment groups were not significantly different with regard to pertinent clinical variables at baseline.

Changes in PASI score and treatment Efficacy

In the present study tazarotene gel 0.1% was effective in the treatment of plaque psoriasis, which was statistically significant ($p < 0.001$). On comparison with mometasone furoate cream 0.1%, there was a significant difference between tazarotene and mometasone cream, which was in favour of mometasone cream both at 8 and 12 weeks. Mometasone cream was superior to tazarotene gel in terms of reduction in PASI scores and overall treatment success.

During the treatment period, tazarotene related adverse events involved only mild to moderate sings and symptoms of local irritation (pruritus and burning) which were consistent with effect of a topical retinoid. These complaints declined by end of treatment week 12 . None of the patients experienced any treatment related systemic adverse effect. As mentioned by Chandratan RAS *et al*. [23], in all animal species studied, tazarotene is rapidly metabolized (half life of 2 to 18 minutes) to its active metabolite tezarotenic acid which in turn is rapidly converted to inactive metabolite resulting in a short elimination half life of 1 to 2 hours. Also no human systemic toxicity was observed after one year long term administration even at the highest dose. This suggests that systemic toxicity is unlikely during long term topical use of tazarotene unlike steroids in humans. The present study was in concurrence with above studies in showing the efficiency of tazarotene gel in treatment of chronic plaque psoriasis but there was a significant difference between tazarotene gel and mometasone cream.

CONCLUSION

A total of 50 patients of chronic plaque psoriasis were included in to the study. Patients belonged to different age groups, both sexes and different economic strata. Majority of patients (62%) were in the age group of 21 to 40 years. In majority of patients (70%), age of onset of disease was between 20 to 40 years with the onset being earlier in males. The duration of disease in most patients (74%) was more than one year, of whom 22% had duration of more than 7 years. The pretreatment clinical variables like age, age of onset, sex, and duration of disease showed no significant differences in both the treatment groups. The male to female ratio was 2.8: 1. Majority of patients were (38%) agriculturists. In the study 44% of patients had winter exacerbations and 4% had summer exacerbations. Positive family history was found in 8% of patients. In both tazarotene and mometasone group, the reduction or difference of mean PASI score both at 8 weeks and 12 weeks of treatment compared to base line was found to be statistically significant ($p< 0.001$). On comparing both the treatment group, there was a significant difference between mometasone group and tazarotene group, which was in favour of mometasone group both at 8 weeks and 12 weeks of treatment ($p<0.001$).To summaries in the present study both tazarotene gel and mometasone cream was found to be effective in reduction of PASI score and clearance of the lesions significantly. The most common adverse effect in tazarotene group was mild to moderate burning sensation (20%). In mometasone group there were 8% of hypopigmentation and 4% of striae. There were no severe adverse reactions in the study.

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