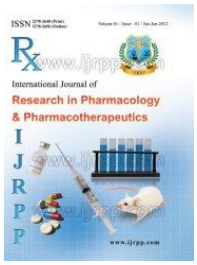
International Journal of Research in Pharmacology & Pharmacotherapeutics



ISSN Print: 2278-2648 IJRPP |Vol.4 | Issue 2 | April-June-2015
ISSN Online: 2278-2656 Journal Home page: www.ijrpp.com

Research article Open Access

Effect of topical tazoretene in comparison to topical corticosteroids on serum proteins in chronic plaque psoriasis

Dr Jagadeesh K[2], Dr Santhosh Kumar M[1], Dr Shreenivas Revankar*[2]

[1]*Assistant Professor; Department Of Pharmacology; J J M Medical College, Davanger, Karnataka, India.*
[2]*Department Of Pharmacology; Shimoga Institute Of Medical Sciences; Shimoga 577201;Karnataka, India*

***Corresponding Author: Dr Shreenivas Revankar**
E-mail id: sprevankar@yahoo.com

ABSTRACT

Tazarotene, the first of new generation receptor selective topical retinoid, currently being investigated and widely used in treatment of mild to moderate psoriasis. Objective: Effect of topical tazoretene in comparison to topical corticosteroids on serum proteins in chronic plaque psoriasis. Meterials and Methods: 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. Serum protein levels were estimated at base line and at 12 weeks.

Results: Both tazarotene gel and mometasone cream were significantly effective. The baseline serum proteins were below normal in both the groups, which significantly increased after 12 weeks of treatment. However there was no significant difference between the two treatment groups on serum proteins.

Interpretation and Conclusion

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.

INTRODUCTION

The enigma in the pathogenesis of psoriasis however is whether the disease is primarily one of keratinocytes or of the immune system.[1] though a major genetic component is present in psoriasis, the pattern does not follow a simple mendelian mode of inheritance. Psoriasis is often believed to be initiated or exacerbated by stressful life events.[2] It is extremely variable in its duration and course. Histologically[3], it is characterized by hyperkeratosis and parakeratosis, absent granular layer, suprapapillary epidermal thinning, elongation of reta ridges, presence of munro micro abscesses and spongiform pustules of kogaj[4]. As rightly commended by shelly and shelly "psoriasis is a diagnostician's delight as it has an honest, forth ring portrait, just a glance is enough to diagnose the disease 2 most of the time". But when it comes to the management it is equally difficult to select a proper modality many a times[5].

The various treatment modalities available are as follows. Phototherapy[6]: it is effective in treatment of psoriasis, UVB in the range (290-320nm) is optimal. Thick and scaly horny layer of untreated psoriatic

lesions screen most of UVB radiations. So it is essential to remove the scales with soap and water prior to exposure to sun and UVB lamp. Patient is then exposed to mid-day sunlight daily or too undergo UVB exposure thrice a week.

Topical steroids

Clobetasol propionate (0.05%) tenovate or betamethasone dispropionate is effective in psoriasis. They act by inhibiting mitosis and inflammation. Side effects of steroids are atropy, striae, telangeectasia, milia, folliculitis, infection and suppression of HPA axis.

Coal tar: inhibit DNA synthesis.sensitise the skin to long wave (UVA) and are effective in psoriasis

Salicylic acid

It is a keratolytic agent used in 3-6% concentration causes softening of horny layers and shedding of scales. Psoriatic ointment comprising of crude coal tar6%, salicylic acid 3%and ammoniated mercury 1% is useful in treatment of psoriasis.

Anthralin (dithranol)

Acts directly on the stem cell population of eridermis. relese of hydrogen atom from 10-methylene group in anthralin initiate the formation of biologically active free radicals. Dithranol inhibits key enzymes like glucose-6-phosphate dehydrogenase. The drugs commonly employed for systemic therapy are corticosteroids. PUVA, methotrexate and retinoids.

Systemic steroids[2,5]

Have no place in management of plaque psoriasis because of risk of conversion to pustular form. Once the patient goes into remissions other definitive treatments like methotrexate or retinoids should be introduced so that steroids can be withdrawn.

Photo chemotherapy (PUVA)[1,6]

The different psoralene preparations are basic psoralene 8-methoxy psoralene and 4, 5, 8-trimethyl psoralene. Two hours after administration of psoralene exposed to sunlight .average number of exposures required is between 20-25.PUVA is highly effective modality of treatment. The important side effects are nausea, erythema, burns and blisters. Methotrexate is a folic acid antagonist. It slows the mitotic activity by reducing DNA synthesis. It also inhibits granulocyte and monocyte chemo taxis. Its anti-inflammatory effect is partially responsible for anti-psoriatic action. Side effects associated with methotrexate are nausea, abdominal discomfort vomiting fatigue and headache.it may also cause bone marrow suppression leading to anaemia, leucopenia and thrombocytopenia, most serious toxic effect is hepatotoxicity.

Retinoids[7]

Etretinate is a synthetic derivative of vitamin A is useful in management of pustular and erythrodermic psoriasis.it is associated with correction of abnormal polyamine metabolismor leucocyte migration.it also inhibits inflammation, proliferation and terminal differentiation. retinoids also have a direct action on keratinocytes.it is a potentially a toxic drug causes mucocutaneous dryness of oral and nasal mucosa, conjunctivitis, dryness of skin, acral fragality and hair loss.it should not be administered to patients with obesity, diabetes mellitus, heavy smokers alcoholics and hypertensives.it is a teratogenic and is excreted very slowly from the body. The third generation retinoids, arotenoids may produce rapid clearance of psoriasis than etretinate.

Cyclosporine[1,8]

Psoriasis is associated with increased T-helper to suppressor cell ratio and decreased suppressor cell activity. cyclosporine selectively inhibits T-helper cell production of interleukin-2, while allowing increase of suppressor T-cell population .important side effects are tremor, headache, hypertrichosis, hypertension, gingival hyperplasia, arthralgia, myalgia and increased risk of malignancy.

MATERIALS AND METHODS

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 contraceptives, evidence of hepatic or renal impairment and other skin infections which can be misleading. 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.[9] Liquid paraffin was also advised for local application for prevention of dry skin. Each patient underwent biochemical tests like serum proteins,

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.

a. Blood investigations were repeated along with biochemical tests to estimate the serum protein levels.

b. 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. 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: OCCUPATION OF PATIENTS

Occupation	Group 1		Group II		Total	
	No	%	No	%	No	%
House wife	7	28	4	16	11	22
Agriculture	9	36	10	40	19	38
Coolie	5	20	4	16	9	18
Business	1	4	4	16	5	10
Student	3	12	3	12	6	12
Total	25	100	25	100	50	100

In the present study psoriasis was most frequently among agriculturists (38%) followed by house wives (22%) coolies (18%) students (12%) and business men (10%).

TABLE -3: HABITS

Habits	Group 1		Group II		Total	
	No	%	No	%	No	%
Smoking	7	28	10	40	17	34
Alcohol	5	20	5	20	10	20
Absent	13	52	10	40	23	46
Total	25	100	25	100	50	100

In the present study 28% of the patients had the habit of smoking in group 1 and 40% in group 2.the percentage of alcoholics were 20% in group 1 and 20% in group 2 .the overall percentage of smokers and alcohol consumption was 34% and 20% respectively.46% of the patients in the study had no habit of smoking or alcohol consumption.

TABLE -4: CHANGES IN SERUM PROTIENS

Groups	Particulars	Base line	12 weeks	Difference
	Mean	4.62	5.01	0.38
	±SD	1.01	1.04	0.28
Group-I	t*	-	-	6.91
	P-value	-	-	<0.001 HS
	Mean	4.68	5.18	0.50
	±SD	0.84	0.74	0.31
Group-II	t*	-	-	8.11
	P-value	-	-	<0.001 HS
	Mean Diff	0.04	0.14	0.12
I Vs II	t*	-	-	1.40
	P-value	-	-	0.17.NS

Group 1 (tazarotene)

The baseline serum a protein in this group was found to be lows, a mean of 4.62 mg% post treatment at the end of 12 weeks it had increased to mean of 5.01 mg% this increase in serum proteins after treatment was found to be statistically significant P<0.001.

Group 2 (mometasone)

The baseline serum a protein in this group was found to be lows, a mean of 4.68 mg%. post treatment at the end of 12 weeks it had increased to mean of 5.18mg%.this increase in serum proteins after treatment was found to be statistically significant P<0.001.

Group 1 vs group 2 though there was a significant increase of serum proteins in both the groups ,there was no significant differences between both the treatment groups at 12 weeks on rise in serum proteins P>0.05

TABLE -5: ADVERSE EFFECTS

Adverse effects	Group 1		Group II		Total	
	No	%	No	%	No	%
Burning sensation	5	20	-	-		
Hypopigmentation	-	-	2	8	8	16
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 reaction in the study was 16% of patients.

DISCUSSION

AGE OF ONSET

In the present study majority of patients had onset of the disease between 21 to 30 years (40%) followed by 30% of patients in age group of 31 to 40 years. Mean age of onset in the study was 34. 65 years, 35.84 in females and 34.24 years in males. Mehta et al[10]observed the onset of disease was highest between 21 to 30 years (36%). Inderjeet Kaur et al[11] reported the mean age of onset for females was 29.34 years and for males 36.9 years. [12] The present study showed similar results to above studies though the ages of onset in males were higher.

OCCUPATION OF PATIENTS

In the present study psoriasis was seen most frequently in agriculturists (38%) followed by house wives (22%), coolies (18%), students (12%) and businessmen (10%). Sharma and Sepaha[13] reported highest incidence of frequency in farmers (23.33%). Thus the present study correlates well with study of Sharma and Sepaha. [14] The highest incidence among agriculturists may be due to occupational trauma and higher number of agriculturists in this part of the state.

HABITS

In the present study 34% were smokers and 20% were alcoholics. Sharma and Sepaha[13] reported that 53.37% of patients had habit of smoking and 30% had the habit of alcohol consumption. Mills et al[15] in their study reported that 46.2% of psoriatic patients had the habit of smoking. The higher incidence of smokers in the present study as in the above studies indicate the adverse effects of smoke, which may result from oxidative damage to critical biological substance[16] Heavy alcohol consumption in men may increase risk of trauma which may affect psoriasis. It may also be a symptom of stress and lead to reduced therapeutic compliance.

CHANGES IN SERUM PROTEINS

Negative nitrogen balance mainly consisting of decrease in serum albumin is usually seen in psoriasis, exfoliative dermatitis and vesiculobullous disorders resulting in protein loss due to scaling.[1, 17] In the present study the baseline serum protein was lower than normal of 6.4-8.3 gm% in both the tazarotene group (4.62 gm%) and mometasone group (4.68gm%). At the end of treatment at 12 weeks the serum proteins was significantly increased in both the treatment groups (p <0.001). However on comparison of both the treatment groups, the rise in serum proteins levels at 12 weeks of treatment did not show any significant difference. Thus the effect of both tazarotene and mometasone was same on rise in serum proteins post-treatment. [18] Kanthraj GR et al[17], have mentioned that various authors have reported

the amount of scale lost leading to protein loss during exfoliation. The scale lost per unit area was significantly higher in psoriasis than in eczema and drug interactions. This is possibly due to high cell turnover in psoriasis. . Disturbance in protein metabolism usually occurs due to protein loss from skin and gastrointestinal tract. When the scaling is severe a negative nitrogen balance can occurs causing hypoalbuminemia, edema and loss of muscle mass. The present study shows decrease in serum proteins at baseline in both the groups in concurrence with above studies, though there was no sign of negative nitrogen balance. There was also a significant increase in serum proteins in both treatment groups at end of 12 weeks; however they did not differ significantly from each other. During the treatment period, tazarotene related adverse events involved only mild to moderate signs and symptoms of local irritation (pruritus and burning) which were consistent with effect of a topical retinoid[19]. These complaints declined by end of treatment week 12. None of the patients experienced any treatment related systemic adverse effect. Weinstein GD et al[20] in their dose and regimen ranging study revealed that tazarotene 0.1% or 0.05% gel applied once or twice daily was effective in the treatment of plaque psoriasis. Mark lebwohl et al[21] had mentioned that both 0.1% and 0.05% tazarotene gels were safe and effective in the treatment of mild to moderate plaque psoriasis. 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.

SUMMARY AND 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 male to female ratio was 2.8: 1. Majority of patients were (38%) agriculturists. In 34% of patients there was history of smoking and 20% were alcoholics. The baseline serum proteins in the treatment groups, tazarotene (4.62 mg%) and mometasone (4.68 mg%) was found to be below normal. The increase in serum proteins after treatment for 12 week in both the groups, tazarotene (5.01mg%) and mometasone (5.18mg%) was found to be statistically significant ($p<0.001$). Though there was a significant increase in serum proteins at end of 12 weeks in both the groups, there was no significant difference between the 93 treatment groups at 12 week ($p> 0.05$). Thus both the drugs had equal effect on increase in serum protein.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.

REFERENCES

1. Christophers E, Mrowietz U. Psoriasis. In: Freeberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SI, editors. Fitzpatrick's dermatology in general medicine. 6th Edn, Vol.1, New York: McGraw Hill; 2003. p.407-27.
2. Farber EM. The language of psoriasis. Int J Dermatol 1991; 30(4): 295-302.
3. Farber EM, Peterson JB. Variations in the natural history of psoriasis. Calif Med 1961; 95: 6-11.
4. Fry L. Psoriasis. Br J Dermatol 1988; 119: 445-61.
5. Pusey WA. History of dermatology. In: Charles C, editor. Springfield IL. 1933. p.223.
6. Camp RDR. Psoriasis. In: Champion RH, Burton JL, Burns DA, Breathnach SM, editors. Textbook of dermatology. 6th Edn. Vol.12, London: Blackwell Science; 1998. p.1589-649.
7. Eugene M, Palo AHO. History of treatment of psoriasis. J Am Acad Dermatol 1992; 4: 640-45.
8. Ronald M, Roxberg AC.Psoriasis.In: Roxberghs common skin disease. 17 Edn, Londen: Arnold 2003.p.128-42.
9. Lebwohl M, Alis. Treatment of psoriasis. Part 1. Topical therapy and phototherapy. J Am Acad Dermatol 2001; 45: 487-98.
10. Mehta TK, Shah RN, Marquis LA. Study of 300 cases of psoriasis. Indian J Dermatol Venereol Leprol 1976; 42(2): 67-69.

11. Kaur I, Kumar B, Sharma VK, Kaur S. Epidemiology of psoriasis in a clinic from North India. Indian J Dermatol Venereol Leprol 1986; 52: 208-12
12. Roenigh HH, Aurebach R, Maibach H. Methotrexate guidelines revised. J Am Acad Dermatol 1982; 6: 145-55.
13. Sharma TP, Sepaha GU. Psoriasis – A clinical study. Indian J Dermatol Venereol 1964; 30(5): 191-203.
14. Butaky L, Weinstein G. The therapy of moderate to severe psoriasis with methotrexate. In: Weinstein G, Gottlieb A, editors. National psoriasis foundation. Therapy of moderate to severe psoriasis. Harber and Flora Inc ; 1993. p.75-93. 105
15. Mills CM, Srivastav ED, Harvey IM, Swiff GL, Newcombe RG, Holt PS et al. Smoking habits in psoriasis a case control study. Br J Dermatol 1992; 127:18-21.
16. Naldi L, Peli L, Parazini F. Association of early – stage psoriasis with smoking and male alcohol consumption. Arch Dermatol 1999; 135: 1479-84.
17. Kantharaj GR, Srinivas CR, Devi PU, Ganasoundari A, Shenoy SD, Deshmukh RP et.al., Quantitative estimation and recommendation for supplementation of protein lost through scaling in exfoliative dermatitis. Int J Dermatol 1999;38:91-5.
18. Bos JD, Melinardi, Joost TV, Heule F, Powles AV, Fry L. Use of cyclosporine in psoriasis. The Lancet 1989; 23/30: 1500-03.
19. Moy RL, Timothy P, Kingston P, Lowe NJ. Isotretinoin Vs Etretinate therapy in generalized pustular and chronic psoriasis. Arch Dermatol 1985; 121: 1297-301.
20. Weinstein GD, Krueger GG, Lowe NJ, Duvic M, Freidman DJ, Jegasothy BV et.al. Tazarotene gel, a new retinoid for topical therapy of psoriasis: vehicle controlled study of safety, efficacy and duration of therapeutic effect. J Am Acad Dermatol 1997; 37:85-92.
21. Lebwohl M, Ast E, Cullen SI, Hong SR, Kulpshorten CL et al. Once daily tazarotene gel verses twice daily flucinocide cream in treatment of plaque psoriasis. Am Acad Dermatol 1998; 38:705-11. 107.