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A CLINICAL STUDY TO EVALUATE THE EFFECT OF TOPICAL TAZAROTENE IN THE TREATMENT OF PLAQUE TYPE PSORIASIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Topical retinoids generally are ineffective or too irritating to be used in psoriasis. Tazarotene is a novel third generation retinoid whose effect in plaque type psoriasis is still under debate. The present study was undertaken to find the efficacy and safety of topical tazarotene in patients with chronic plaque type psoriasis during treatment and post treatment periods. Patients who met the inclusion criteria were included in the treatment group after obtaining informed consent. The patients were given topical tazarotene for 12 weeks. Severity of lesions was graded based on ESI (Erythema.Scaling,Induration), PASI(Psoriasis Area and Severity Index) and PGA(Physician Global Assessment) scoring at baseline, 2, 4, 6, 8, 10 and 12 weeks. Both serious and non-serious adverse events were noted during each follow up. Post treatment follow up was done at 16th week. The statistical analysis was performed using SPSS (Statistical package for social sciences) and analysis was done using unpaired t test, chi- square test and ANOVA. The reduction in PASI in tazarotene treated group was 62.69% (p value<0.05).About 37.5%, 56.3% and 6.3% of tazarotene treated patients showed marked improvement, almost clear lesions and clear lesions in PGAI respectively. A reduction of 72.9%, 56.7% and 79.1% in intensity of erythema, scaling and induration was seen at the end of 12 weeks of therapy. No serious adverse event was seen throughout the study period. There was also a sustained therapeutic effect during post treatment period. Topical tazarotene is a safe, effective and well tolerated therapy for patients with mild to moderate chronic plaque type psoriasis.

Key words: Tazarotene, PASI, PGA, ESI scoring, Plaque type psoriasis.

INTRODUCTION

Psoriasis is an immune mediated genetically determined common dermatological disorder which affects the skin, nails, joints and has various systemic associations. (NSF, *online database*). This disease has got a great impact on the patient's quality of life and economy. (Badia *et al*, 1999) The incidence and prevalence of psoriasis is on rise in both developed as well as developing countries. Prevalence studies of psoriasis in India are mostly hospital based varying from 0.44 to 3.8%.

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The prevalence and morbidity due to psoriasis is steadily increasing due to the modern stressful life style, lack of physical activity and increased incidence of metabolic diseases like diabetes mellitus, hypertension, hyperlipidemia etc. (Bos JD *et al*, 1993) It is twice more common in males compared to females, and most of the patients present during their third or fourth decade of life. Among the psoriasis patients, the most common type is plaque type disease which accounts for 93% of the cases, the other types of psoriasis being guttate type psoriasis, pustular psoriasis, inverse psoriasis, erythrodermic psoriasis etc.

Psoriasis has been graded based on their severity as mild, moderate and severe. Among these the mild form

of psoriasis is more commonly seen and it accounts for 65% of the psoriasis cases. Currently there is no cure for psoriasis but various treatments can help to control its symptoms. (Centers for disease control, *online database*). There are a number of different treatment options for psoriasis (Duvic *et al*, 1998). Typically topical agents are used for mild disease, phototherapy for moderate disease and systemic agents for severe disease (Schon MP *et al*, 2005). The topical agents available for treatment of mild to moderate psoriasis are- coal tar, dithranol, corticosteroids, vitamin D_3 analogues, and retinoids (Albrecht L *et al*, 2011). The mechanism of action of each of these topical agents is different; but they all help to normalize skin production and reduce inflammation (Ingram JT, 1953). Retinoids are suitable for treatment of plaque type psoriasis but however previous studies have shown reduced effect and severe irritation as side effect (Marks R *et al*, 1997). Tazarotene is a topical third generation retinoid whose effect in chronic plaque psoriasis is still not fully understood (Menter *et al*, 2000). Hence we undertook this study to evaluate the efficacy and safety of tazarotene in treatment of patients with chronic plaque type psoriasis.

Objective of the study

To determine the efficacy and safety of topical tazarotene 0.1% once daily, for patients with mild to moderate chronic plaque type psoriasis during treatment and post treatment periods.

METHODOLOGY

Study Design

A prospective open label study of topical tazarotene in plaque type psoriasis conducted at the outpatient clinics of Department Of Dermatology, Sri Ramachandra Medical College and Research Institute, Porur, Chennai during the period October 2012 to august 2013 after procuring approval from institutional ethical committee.

Patients

Informed consent was obtained from all patients before entering the study. All the eligible participants who took part in the study were informed about their freedom to withdraw from the study at any time without giving any reason and while doing so they will not be denied the option of obtaining quality medical care in the same institute. Case report forms were prepared for each patient and kept with the investigator.

Study Medications

Topical Tazarotene 0.1% ointment was purchased from whole sale stockiest (brand name: tazret, manufacturer: Glaxosmith pharmaceuticals) and supplied to the study participants during each scheduled visit along with compliance card

Duration of the study

The treatment duration is 12 weeks (3months). Post treatment follow up was done during the 16^{th} week.

Mode of Administration

All the study participants were instructed to apply a thin film of the study drug over the psoriatic lesions avoiding application to the normal skin. They were advised to apply the study medications over dried skin in the evening. The patients were also instructed to avoid exposure to excessive sunlight. During the study period other local or systemic medications for treatment of psoriasis were not permitted. In the event of local irritation, only liquid paraffin oil was permitted.

Psoriasis Severity Grading

Severity of psoriasis was graded based on PASI scoring, ESI scoring and Physicians Global Assessment Index.(Feldman SR *et al*, 2005) All the above parameters were assessed on baseline, 2,4,6,8,10,12 weeks and at 16th week (post treatment period)

Laboratory Investigations

Laboratory investigations were done during the baseline visit and 12 th week of the study period. Fasting blood glucose level and HbA1c levels were taken for the patients after 12 hrs of overnight fasting. Skin scraping test was done only for new cases of psoriasis to confirm the diagnosis.

Adverse Events Reporting

All the adverse events observed/complained by the study participants were reported in the case report form along with the information about the severity (mild, moderate or severe) and possible relation to the study medication.

Statistical Analysis

The statistical analysis was performed using SPSS (Statistical package for social sciences) for windows version 16 and was analysed using unpaired t test, chi-square test and ANOVA. Mean and standard deviation was provided for continuous data, while absolute frequencies and percentage were provided for categorical data. P value <0.05 was considered statistically significant. All the analyses were based on modified intention to treat (ITT) principle. Modified ITT population included all the study participants who had completed at least one follow- up visit.

RESULTS AND DISCUSSION

A total of 60 patients were screened, among which only 35 patients were enrolled into the study after meeting the inclusion and exclusion criteria. Baseline demographic profile at the start of the study is shown in table 1. Out of 35 patients, 3 patients were lost to follow

up and 1 patient refused to give informed consent. The mean age of the study participants was 41 with a SD of 6.9 ranging from 34 to 48 years. This is in accordance with the study conducted by G. Swanbeck *et al*, which mentions that the prevalence of psoriasis is more common in the third to fourth decade of life. Most of the study patients were males, which coincides with the previous studies. According to Bedi TR *et al*., males are more likely to present with plaque type psoriasis than females.

Efficacy Profile

PASI Scoring

The mean PASI score was 4.717, 4.500, 4.163, 3.448, 2.991, 2.197, 1.776 and 1.513 at baseline, 2, 4, 6, 8, 10, 12 and 16 weeks respectively as shown in Fig 1. The mean percentage changes from baseline PASI was 4.59%, 11.73%, 26.88%, 36.43%, 53.31%, 62.69% and 68.15% at 2, 4, 6, 8, 10, 12 and 16 weeks respectively. Hence, tazarotene proved to have a sustained effect on psoriatic lesions. This is comparable to the study conducted by GD Weinstein *et al*.

Physicians Global Assessment Scaling

The overall physician's global assessment scaling (PGA) in treated group was done during each follow up visit. The percentage of patients showing mild, moderate or marked improvement during each visit is shown in fig 2-7. At week 2, 20% and 80% patients showed no change and minimal improvement in tazarotene group respectively. At week 4, 82.9% patients showed minimal improvement and 17.1% patients showed moderate improvement in treated group.At week 6, 5.7%, 91.4% and 2.9% patients showed minimal, moderate and marked improvement in treated group respectively. At week 8, 36.4% patients and 63.6% patients showed moderate and marked improvement in tazarotene group respectively. At week 10, 18.2%, 51.5%, 24.2% and 6.1% patients showed moderate improvement, marked improvement, almost clear lesions and clear lesions in tazarotene group respectively. At week 12, 37.5%, 56.3% and 6.3% patients showed marked improvement, almost clear lesions and clear lesions in tazarotene group respectively

ESI Scoring

The mean intensity of erythema in tazarotene group is 1.85, 1.8, 1.25, 0.8, 0.6, 0.4 and 0.4at 0, 2, 4, 6, 8, 10 and 12 weeks of therapy respectively. The mean intensity of scaling in tazarotene group is 1.85, 1.8, 1.3, 1.2, 0.85, 0.8 and 0.6 at 0, 2, 4, 6, 8, 10 and 12 weeks of therapy respectively. The mean intensity of induration in tazarotene group is 2.4, 1.4, 1.25, 1.15, 1, 0.65 and 0.5 at 0, 2, 4, 6, 8, 10 and 12 weeks of therapy respectively (Table 2). The study group showed a reduction of 72.9%, 56.7% and 79.1% in intensity of erythema, scaling and induration respectively at the end of 12 weeks of therapy as shown in Fig 8.

Safety Profile

The study drug was well tolerated. All adverse events encountered by the study participants during the treatment period were captured and assessed for causality. In the tazarotene group 3 patients complained of mild irritation, 2 patients had dry skin and 2 patients had itching. Patients who complained of itching were treated with anti-histamines concurrently. These patients were symptom free after 4-5 days. Patients who had irritation and dry skin were asked to apply liquid paraffin oil (emollient) along with the study drug. There was no systemic effect of drugs encountered in the study. There was no incidence of serious adverse events or discontinuation of treatment due to adverse effects in the treated group.

Table 1. Baseline Patient Characteristics

Parameter		Tazarotene Group n=35
Age (years)		41±6.9
Sex	Male	21 (60%)
	Female	14 (40%)
Mean duration of disease (months)		5±6.7
Smokers		4 (11%)
Alcohol use		3 (9%)
Diabetes mellitus		9
Hypertension		6
Mean body surface area affected		5-15%
PASI score at baseline		4.717±0.9710
ESI score at baseline	Erythema	1.85±0.34
	Scaling	1.85±47
	Induration	2.4±0.69

Table 2. The Mean PASI **Score of the Treatment Group during the Follow Up Visits Starting from the Baseline Visit**

Weeks	0	2	4	6	8	10	12
Erythema	1.85	1.8	1.25	0.8	0.6	0.4	0.4
Scaling	1.85	1.8	1.3	1.2	0.85	0.8	0.6
Induration	2.4	1.4	1.25	1.15	1	0.65	0.5

Figure 1.The mean PASI score of tazarotene treated patients during each visit starting from baseline to 12 weeks of therapy

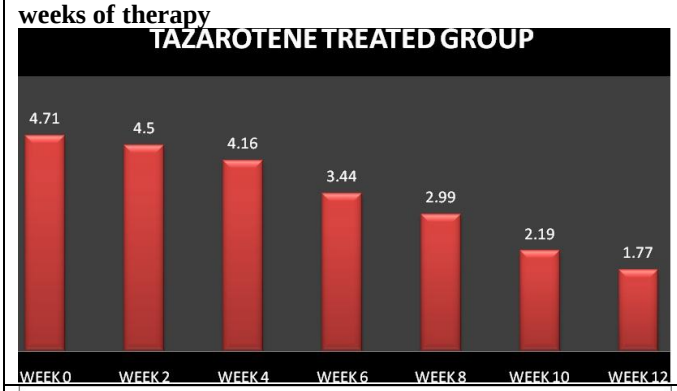
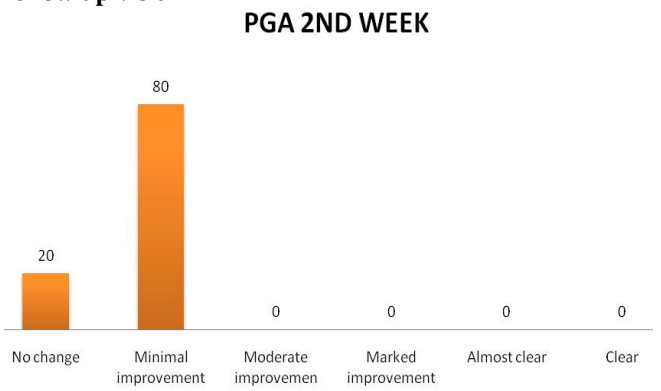
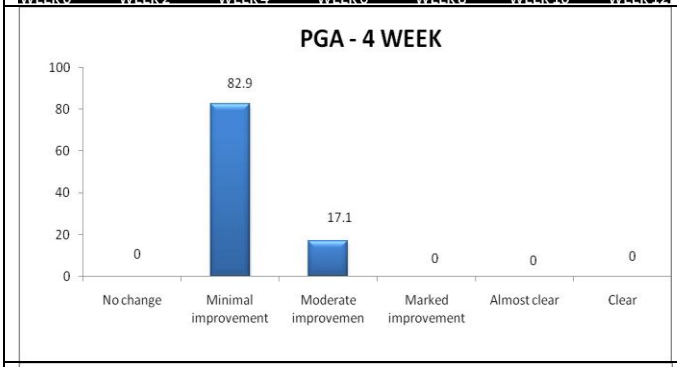
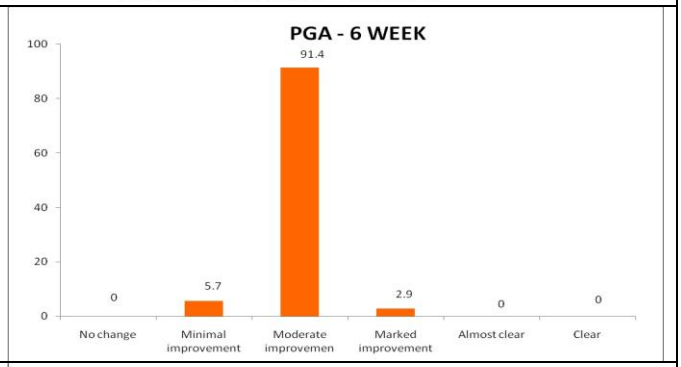
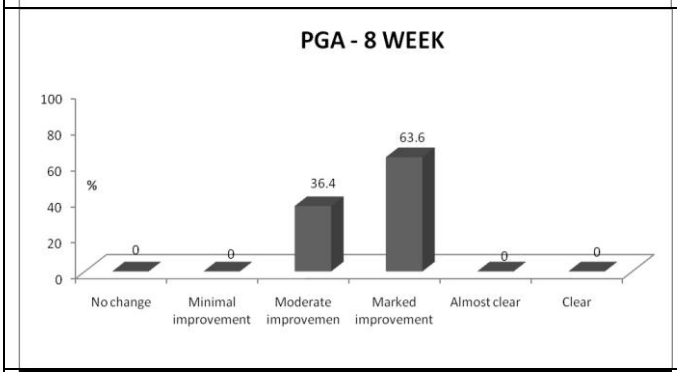


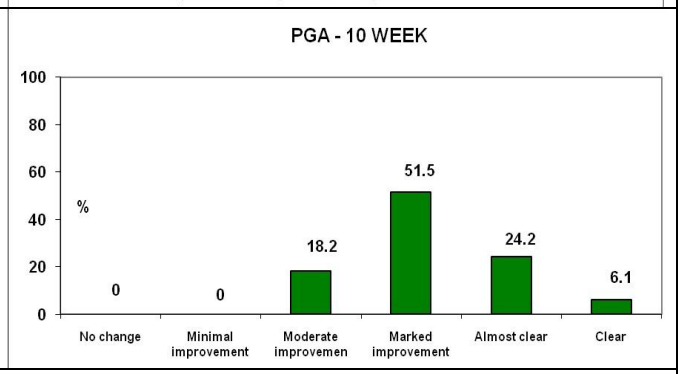
Figure 2-7. Percentage improvement in PGA at each follow up visit











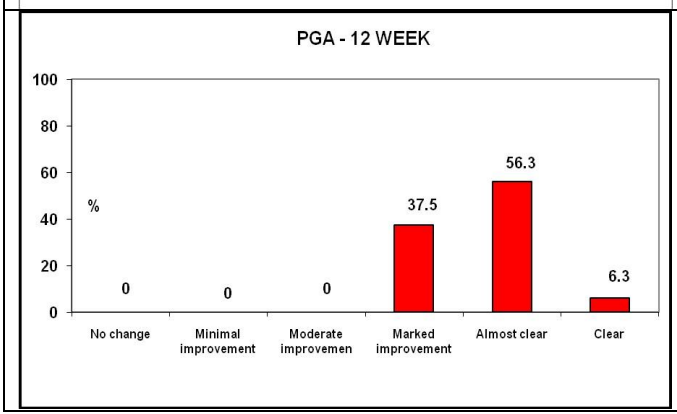
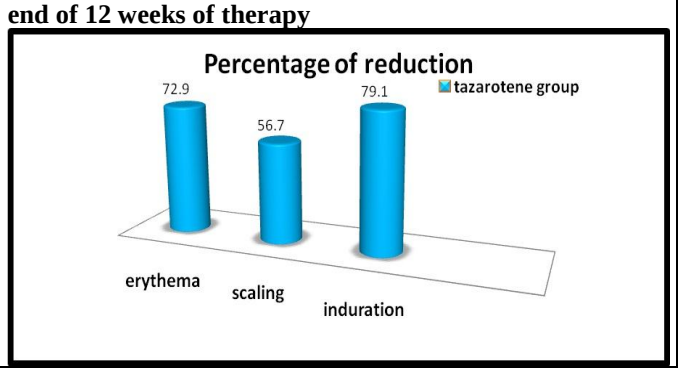


Figure 8. The percentage of reduction in ESI score at the end of 12 weeks of therapy



CONCLUSION

To conclude, topical tazarotene showed good improvement in PASI, ESI and PGA scoring. It was well tolerated by all patients. It also had sustained effect during the post treatment period.

Thereby, our study proves that topical tazarotene is a safe, effective, well tolerated therapy and a proven alternative to other drugs used in the treatment of chronic stable plaque type psoriasis patients.

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