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CLINICAL REPORT

Comparison of Tazarotene 0.1% Gel Plus Petrolatum Once Daily Versus Calcipotriol 0.005% Ointment Twice Daily in the Treatment of Plaque Psoriasis

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Tazarotene and calcipotriol are both effective in the treatment of psoriasis. An investigator-blind, bilateral comparison of 44 lesion pairs in 19 patients was conducted to evaluate the efficacy, side effects and duration of therapeutic effects of once-daily tazarotene 0.1% gel plus petrolatum with twice-daily calcipotriol 0.005% ointment in plaque psoriasis. It consisted of a 12-week treatment phase, followed by a 4-week post-treatment observation phase. At the end of the treatment phase, tazarotene-petrolatum was as effective as calcipotriol in both objective and subjective overall efficacy assessment. Calcipotriol had a significantly greater effect in reducing erythema than tazarotene-petrolatum at weeks 2–8. At week 16, tazarotene-petrolatum demonstrated a significantly better maintenance effect in all parameters. Local irritation was noted only in tazarotene-petrolatum-treated lesions. Once-daily tazarotene 0.1% gel plus petrolatum was as effective as twice-daily calcipotriol 0.005% ointment in the treatment of plaque psoriasis, but had a better maintenance effect after the cessation of therapy.
Key words: calcipotriol; psoriasis; tazarotene.

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Topical treatments available for plaque psoriasis include emollients, keratolytics, coal tars, anthralin, corticosteroids, vitamin D analogues and tazarotene. Among them, topical corticosteroids are the most commonly prescribed medication (1). Long-term use of corticosteroids is known to have several potential adverse effects, including skin atrophy, telangiectasia, hypertrichosis and systemic absorption with associated adrenal suppression. To avoid the undesired side effects, non-steroid topical agents, calcipotriol and tazarotene, are used as alternatives in psoriasis. However, there are still no reports in the literature comparing the efficacy of the above two topical agents head to head as monotherapy for plaque psoriasis. The aim of our study was to investigate whether topical tazarotene is as effective as calcipotriol in alleviating plaque psoriasis.

MATERIALS AND METHODS

This was a single-centre, prospective, investigator-blind, bilateral comparison study approved by the medical ethics committee of the Veterans General Hospital, Kaohsiung. Written informed consent was obtained from each patient before enrolment in the study and from the patient's parents or guardians if the patient was under the legal age of consent.

Subject selection

A total of 23 Chinese patients with plaque psoriasis (21 men and 2 women; aged 12–80 years, mean age 60.2 years) with 50 target lesion pairs were recruited. The male predominance reflected the patient population of a veteran's hospital. Those who had received oral systemic antipsoriatic treatment within the previous 6 weeks or topical antipsoriatic treatment within the previous 2 weeks were excluded. Other exclusion criteria included exposure to sun or ultraviolet treatments in the previous 4 weeks, a current diagnosis of unstable psoriasis, pregnancy, breast-feeding or uncontrollable systemic disease. Because this was a right-left bilateral lesion comparison study, patients' differences in sex and age were not considered in the treatment comparison.

Calcipotriol 0.005% ointment (Daivonex®, Leo) was applied twice daily to the affected areas on one side of the body, randomly assigned for each patient. On the other side of the body, tazarotene 0.1% gel (Tazorac®, Allergan) was applied once in the evening and petrolatum once in the morning. One to three target lesion pairs were appointed for each patient. All lesion pairs had to be in similar anatomic locations and of roughly equal severity. Each target lesion had to be at least of moderate severity. Scalp and facial psoriasis was neither treated nor assessed.

Assessments

The severity of each of the paired psoriatic lesions was recorded on each visit (weeks 0, 1, 2, 4, 8 and 12 and post-treatment weeks 2 and 4) with the aid of a set of reference photographs whose severity had been agreed among the investigators. Adverse events, if any, were documented on each visit. As in the previous study, we chose to use a 9-point rating scale to evaluate the degree of scaling, plaque elevation and erythema of target lesions (0=none, 1=mild, 2=moderate, 3=severe, and 4=very severe), scored in 0.5-point increments (2). The sum of these scores was calculated. An overall efficacy assessment was made by the patients at the end of treatment using a defined 5-point grading scale as 1=excellent (>75%) improvement, 2=marked (51–75%) improvement, 3=moderate (26–50%) improvement, 4=no (0–25%) improvement, and 5=deterioration (3).

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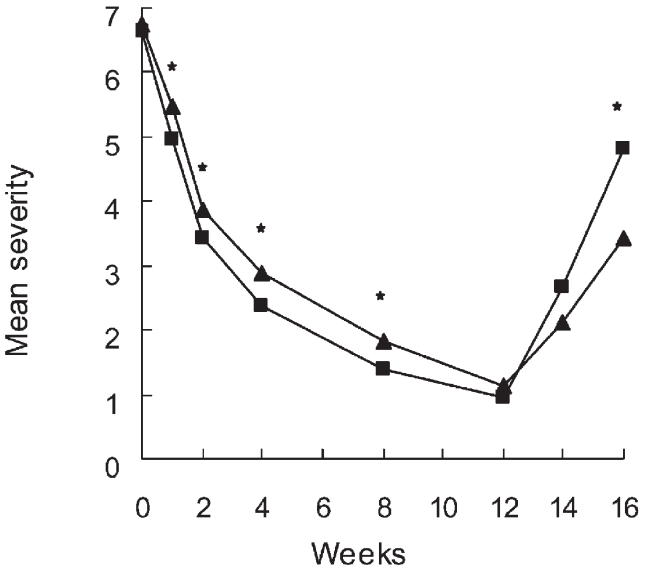

Fig. 1. Mean overall severity during the 12-week treatment phase and the 4-week post-treatment observation phase. *$p<0.05$, tazarotene-petrolatum (▲) versus calcipotriol (■).

Statistical analysis

Severity scores for scaling, plaque elevation, erythema and overall lesional severity were compared at the baseline and across seven time points using the Friedman's test. The post hoc comparisons between the baseline point and the other seven points were evaluated using the Wilcoxon sign rank test. The comparison of various severity scores between tazarotene-petrolatum- and calcipotriol-treated lesion pairs was tested using the Wilcoxon sign rank test. Additionally, the patient's self-reported efficacy of treatment was tested using the Pearson chi-square exact test. A p value <0.05 was considered statistically significant.

RESULTS

Nineteen patients (44 target lesion pairs) completed the treatment phase of the study and were included in the statistical analysis for efficacy. The locations of the target lesions were on legs ($n=21$), arms ($n=13$) and trunk ($n=10$). All of them returned for post-treatment visits up to 4 weeks. Four patients dropped out. The reasons for withdrawal included unacceptable adverse events in three patients (erythema, severe pruritus and burning sensation), all on the tazarotene-petrolatum (T/P)-treated side, and unsatisfactory response in one patient (week 2).

At the baseline, the severity of T/P- and calcipotriol-treated lesions was similar in scaling, plaque elevation, erythema and overall lesional severity. At the end of the 12-week treatment, T/P was as effective as calcipotriol in the reduction of scaling, plaque elevation, erythema and overall lesional severity (Fig. 1). Compared with the baseline, both T/P and calcipotriol showed statistically significant improvements in scaling and plaque elevation after 1 week of treatment (Table I). Erythema deteriorated from the baseline on the T/P-treated side in week 1. Reduction of erythema on the T/P-treated side was first noted in week 2. Compared with calcipotriol, erythema reduced less on the T/P-treated side but the difference became statistically insignificant after 8 weeks of treatment.

Lesional severity scores worsened on both sides during the post-treatment phase. After therapy ceased, T/P maintained the therapeutic effect significantly better in scaling ($p<0.001$), plaque elevation ($p<0.001$), erythema ($p=0.01$) and overall severity ($p=0.007$) at week 16 (Fig. 2). Forty-five adverse events were observed in the T/P-treated lesions, including erythema, burning sensation and pruritus within 1 hour of the topical application of tazarotene. Perilesional erythema was found in 14 T/P-treated target lesions (32%). Itch in 10 patients (23%) and burning sensation in 2 patients (4%) were noted after T/P applications. Folliculitis was found on the periphery of one target lesion treated with calcipotriol. It completely resolved in 1 week after avoiding calcipotriol contact with the normal skin.

The treatment success rates (defined as at least marked improvement) assessed by the patients themselves were 74% on the T/P-treated side and 85% on the calcipotriol-treated side. There was no statistically significant difference between the two sides (Table II).

Table I. *Mean severity of scaling, plaque elevation and erythema (±SD) during the 12-week treatment phase and the 4-week post-treatment observation phase*

	Scaling		Plaque elevation		Erythema	
	T/P	C	T/P	C	T/P	C
Week 0	2.3±0.71	2.2±0.76	2.3±0.72	2.1±0.73	2.2±0.79	2.2±0.80
Week 1	1.5±0.60	1.5±0.65	1.6±0.65	1.4±0.66	2.4±0.97	2.0*±0.97
Week 8	0.5±0.55	0.4±0.51	0.4±0.48	0.3*±0.42	0.8±0.80	0.7±0.72
Week 12	0.3±0.43	0.3±0.49	0.2±0.40	0.2±0.39	0.5±0.71	0.4±0.70
Week 16	1.2±0.87	1.7*±0.66	1.0±0.68	1.6*±0.76	1.1±0.76	1.3*±0.72

*$p<0.05$; significant difference between the group treated with tazarotene-petrolatum (T/P) and that treated with calcipotriol (C) by t-test analysis.

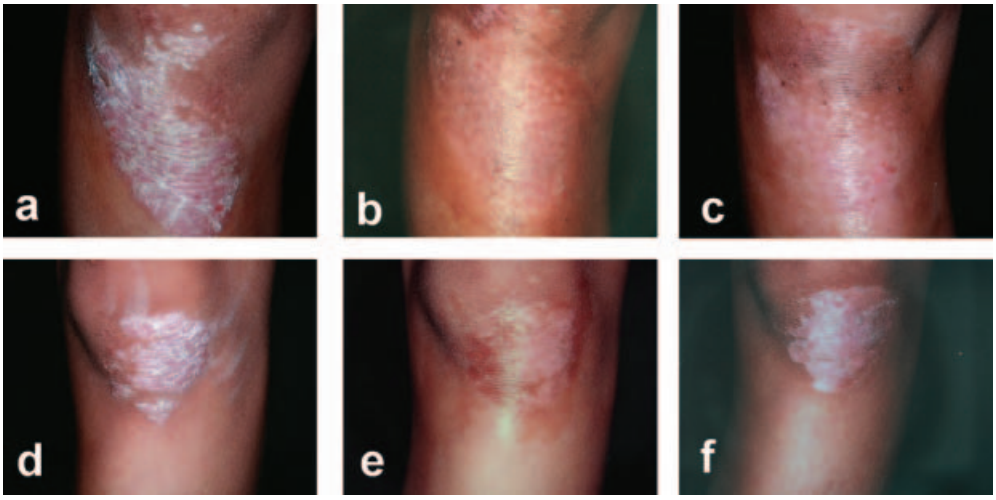

Fig. 2. Clinical response of a target lesion pair at baseline (a, d) and after 12 weeks of treatment with tazarotene-petrolatum (b) or with calcipotriol (e). Tazarotene-petrolatum (c) had a better maintenance effect than calcipotriol (f) after discontinuation of treatment for 4 weeks.

Table II. *An overall assessment of treatment efficacy by patients (%)*

Assessment of treatment	Tazarotene-petrolatum	Calcipotriol	*p**
Excellent improvement	21	32	0.46
Marked improvement	53	53	1.00
Slight improvement	21	15	1.00
No improvement	5	0	1.00
Deterioration	0	0	1.00

**p* values are derived from chi-squares (the value was calculated post Fisher's exact correction).

DISCUSSION

Previous studies had shown that once-daily tazarotene gel plus mometasone furoate cream elicited greater reductions in the severity of psoriasis than twice-daily calcipotriene (4). When combined with narrowband UVB, tazarotene and calcipotriol had similar therapeutic effects (5). In addition, tazarotene plus corticosteroid provided a further 35% reduction of overall severity in psoriatic patients already treated with calcipotriene with or without corticosteroid (6, 7). Our study demonstrated that tazarotene 0.1% gel plus petrolatum was as effective as calcipotriol 0.005% ointment for plaque psoriasis after 12 weeks of treatment. Petrolatum, as an emollient, is known to help barrier function and to have a therapeutic effect in psoriasis (8). However, compared with tazarotene monotherapy, tazarotene plus emollient had little influence on the overall severity of plaque psoriasis except decreased plaque elevation (9). The reasons why the side treated with tazarotene 0.1% gel was additionally applied with petrolatum once in the morning were to counterbalance the difference in application frequency and preparation nature. It would also be interesting to make a direct comparison between tazarotene and calcipotriol as monotherapy. Tazarotene gel was reported to be effective in the treatment of plaque psoriasis as early as treatment week 1 (10). Patients generally experienced a clinical response within 4 weeks after starting tazarotene treatment (11). As for calcipotriol, the response could frequently be seen after 1 week of treatment, reaching the maximum improvement in 6–8 weeks (1, 12). Regarding speed of action, our results showed that calcipotriol achieved a reduction in severity (erythema, scaling, plaque elevation and overall severity) more rapidly than tazarotene-petrolatum.

Compared with fluocinonide, tazarotene could lead to a longer remission of plaque psoriasis (13). Bowman et al. (2) demonstrated that remission could be maintained for up to 8 weeks after the discontinuation of tazarotene. As for calcipotriol, relapse occurred in a mean of 7 weeks after the cessation of therapy (12). In our study, all the lesions worsened after the discontinuation of treatment but tazarotene-petrolatum had a better maintenance effect than calcipotriol.

Local irritation was the most frequent adverse event associated with tazarotene use; it occurred in 30% of patients (10). Concomitant use of emollients or corticosteroids was reported to reduce the adverse events associated with tazarotene use and to increase patients' satisfaction (9). Combined with petrolatum, tazarotene was found to be irritating in up to 35% of the lesions in our study. Irritation was reported in between 9% and 31% of Caucasian patients treated with calcipotriol (14–16). A similar result was found in Thailand (17). In our observations, irritation was not found in any calcipotriol-treated lesions except one with folliculitis. In patients switching treatment from calcipotriene plus corticosteroid to tazarotene plus corticosteroid, the proportion of patients who were satisfied with the treatment increased from 17% to 74% (6, 7).

Instead of patients' satisfaction, treatment efficacy either with tazarotene-petrolatum or with calcipotriol was investigated in our study. The lower, although not statistically significant, success rate on the tazarotene-petrolatum side might be related to tazarotene-induced irritation. Erythema, as a common side effect and one of the three parameters for severity assessment, might have had more visual impact on patients when they evaluated treatment success.

In conclusion, tazarotene-petrolatum and calcipotriol have similar therapeutic effects as monotherapy agents in treating plaque psoriasis. However, tazarotene has more initial irritation but a better maintenance effect. Therefore, a switch therapy, first with less-irritating calcipotriol and then shifting to tazarotene, may be a better strategy in treating plaque psoriasis.

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