Combination phototherapy of psoriasis with tazarotene and UVB

G. Stinco, G. Bragadin, V. De Francesco, A. Frattasio and P. Patrone

SUMMARY

The addition of oral retinoids to phototherapy has shown to enhance both the efficacy and rapidity of psoriatic lesion clearance when compared to phototherapy alone. Tazarotene is the first available topical retinoid developed for the treatment of psoriasis. In the present study, a total of 20 patients with plaque psoriasis were randomly assigned to one of the two treatment groups: tazarotene 0.1% gel plus UVB phototherapy or UVB phototherapy alone. During the two months of the study only 10 patients applied a thin film of tazarotene gel 0.1% to all psoriatic lesions once daily, in the evening. All patients were exposed to UVB three times weekly. Patients were evaluated for tolerability and global response to treatment using the Psoriasis Area and Severity Index (PASI) at days 0, 10, 20, 30, 40, 50, 60. At baseline the mean PASI in the tazarotene plus UVB group was 8.6, while in the other group it was 8.3. At the end of the study the mean PASI in the tazarotene plus UVB group was 4.6, while in the other group it was 5.4. All treatments were generally well tolerated and the incidence of undesired side effects was low.

Background

Psoriasis is a chronic T-cell-mediated inflammatory skin disease which can be treated with topical medication, phototherapy or systemic drugs. A subgroup of psoriatic patients does not respond to monotherapy and needs a combination therapy. In other cases it is the doctor who chooses the combination therapy to reduce the doses of each treatment used. The addition of oral retinoids to phototherapy has shown to enhance both the efficacy and rapidity of psoriatic lesion clearance when compared to phototherapy alone (1). Tazarotene is the first available topical retinoid developed for the treatment of psoriasis. It appears to offer antipsoriatic efficacy without many of the toxicity problems related to systemic therapy (2, 3). So far no studies are available on the combination therapies with this topic drug. The aim of the present study was to evaluate the efficacy and tolerability of the combination therapy with Tazarotene 0.1% gel plus UVB phototherapy compared to UVB phototherapy alone.

KEY WORDS

tazarotene, UVB phototherapy, psoriasis, side effects

Patients and methods

A total of 20 patients with plaque psoriasis having a Psoriasis Area and Severity Index (PASI) score between 5 and 15 and aged from 18 to 70 years were enrolled in this study. Exclusion criteria included patients treated with systemic or topical antipsoriatic drugs in the previous 4 weeks, or who had made use of phototoxic or photosensitizing drugs; those affected with serious cardiac, hepatic and kidney diseases, disorders of the hematopoietic system, psychiatric disorders and those who had a past history of cancer or progressive cancer disease, photodermatitis, or were pregnant women. Patients fulfilling the enrolment criteria were 13 males and 7 females, aged between 20 and 68 years, mean age being 48 years.

Patients were randomly assigned to one of the two treatment groups: 10 patients were treated with Tazarotene 0.1% gel plus UVB phototherapy and 10 patients underwent UVB phototherapy alone. The 10 patients of the first group applied a thin film of tazarotene gel 0.1% to all psoriatic lesions once daily in the evening, excluding those on the face, head, flexor, and intertriginous areas. All patients were exposed to UVB three times weekly. The study lasted 2 months. Patients were evaluated for global response to treatment using the PASI at days 0, 10, 20, 30, 40, 50, 60. At baseline the mean PASI in the Tazarotene plus UVB group was 8.6, while in the UVB alone group was 8.3. Haematological tests and ECG were performed on the first visit and at the check-up at the end of the study. Patients were recommended not to use other psoriasic treatments and to avoid sun exposure. Use of hydrating products was allowed.

The grade of tolerance was estimated on the basis of patients' comments and on the survey of the intensity of cutaneous irritation signs observed during clinical examinations. Treatment efficacy assessment was performed by means of the PASI. Statistical significance of PASI reduction related to times was evaluated by means univariate and multivariate analysis of variance.

Results

An improvement of the clinical picture was observed in all patients. The PASI was progressively reduced both in the patients who had been treated using the combination therapy and in those who had been submitted to the UVB exposure alone (Fig. 1 and Tab. 1). By the end of the study, in the group of patients treated with tarazotene plus UVB, the mean PASI changed from the initial 8.6 to the final 4.6, while the mean PASI in the UVB alone group changed from the initial 8.3 to the final 5.4 (univariate and multivariate analysis of variance: F=1.38 and P=0.30).

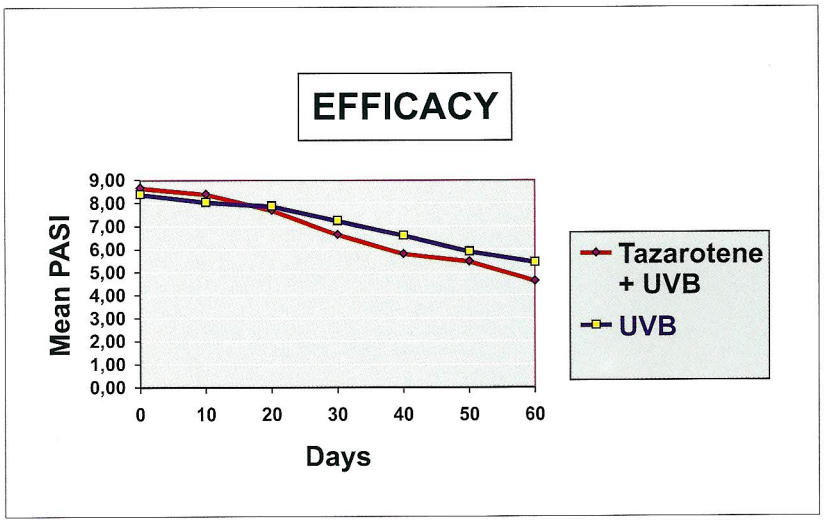

Figure 1. Mean PASI reduction in the 2 study groups.

No variations worthy of note were observed either in the haematological tests or in the ECG. All treatments were generally well tolerated and the incidence of undesired side effects was low. A diffused erythema was observed in 2 patients on one occasion after UBV exposure; 2 patients lamented itching and 1 patient reported a burning sensation on the sites of the tazarotene gel application. There were no dropouts owing to a treatment related adverse event.

Discussion

Tazarotene is the first of a new generation of acetylenic retinoids, which has proven to be efficacious in the treatment of mild-to-moderate plaque psoriasis (2, 3). Tazarotene gel is cosmetically acceptable, is generally well tolerated and is minimally absorbed systemically, with adverse events limited to local irritation (2, 3). Topically applied, in preclinical toxicity studies, it was neither teratogenic nor carcinogenic and was not sensitizing, phototoxic, or photosensitizing (4, 5).

The cosmetic acceptability, the modest local side effects and the absence of systemic adverse events were confirmed in the present study. Tazarotene did not prove to be phototoxic if applied in the evening before UVB exposure. The diminution of the PASI was observed to be slightly higher in the group of patient

Table 1. The variation of PASI observed in the patients examinated.

Patient	Sex	Age	UVB	UVB+ tazarotene	Baseline PASI	1° PASI	2° PASI	3° PASI	4° PASI	5° PASI	6° PASI
ZL	M	54	*		7,3	7	7	6,8	6,3	5,3	5
CC	F	58		*	7,1	8,5	8,9	4,4	4,2	3,9	3
ML	M	57		*	5,1	4,1	3,2	3,4	2,6	2,6	1,2
SR	M	38	*		6,6	6,8	6,1	5,6	5,2	4,6	4,2
BM	F	40	*		8,1	8,6	8,1	7,6	6,5	5,2	4,1
GM	M	37		*	6,4	5,6	6	5,2	5,6	5,2	4,9
CV	M	47	*		14,2	13,3	14	13,4	13,2	13,2	13,2
CP	M	54	*		11,5	10,8	10,2	10	9,5	8,7	8,6
BP	M	29		*	14,7	14,2	12,1	10,9	10,2	9,6	8,2
BR	F	20	*		8,4	7,7	7,2	6,5	6,3	5,2	4,9
CA	F	34	*		5,3	4,7	4,3	2,8	2	2	1,4
ML	M	68		*	14,8	17,2	16,5	12,7	8,2	8	5,7
LG	F	37	*		7,6	7,4	7,8	6,7	5,7	4,3	3,5
DM	M	44		*	9,4	8,1	8,4	8,2	7,7	7,2	6,8
SD	M	53	*		7,1	7	6,7	6,4	6,2	5,9	5,8
VD	M	36		*	5,2	4,8	4,6	4,2	4,1	3,7	3,4
CR	F	39		*	9,9	8,5	6,3	6,8	6	5,7	5,1
CM	M	58	*		7,8	7,2	7,4	6,7	5,3	4,9	3,9
FD	F	44		*	7,3	6,6	5,4	5,6	5,1	4,9	4,7
RU	M	50		*	6,8	6,4	5,6	5,1	4,5	4,1	3,4

who had applied the topic compared to those who had been treated with the phototherapy alone, but the difference was not significant. The small sample of patients studied is insufficient to allow us to venture a definite judgement on the efficacy of the combination therapy compared to the phototherapy alone. We hope that the performance of a further study using a more significant number of patients will enable to determine whether it is possible to reduce both the quantity of the topic drug and the dose of the UVB in the combination therapy and to observe how long the benefits obtained last once the therapy is suspended. This is the only way to determine, with the least possible risk of error, whether the association of tazarotene gel plus UVB phototherapy is a therapy, which opens up new horizons in the treatment of psoriasis.

Presently, we can only conclude that the addition of tazarotene to UVB phototherapy seems effective in the management of psoriatic lesions. The low incidence of adverse events seems to suggest that this combination therapy can be taken into consideration as a possible treatment of psoriasis.

REFERENCES

1. Lowe NJ, Pristowsky JH, Bourget T, et al. Acitretin plus UVB therapy for psoriasis. Comparison with placebo plus UVB and acitretin alone. J Am Acad Dermatol 1991; 24: 591-4.

2. Weinstein GD, Krueger GG, Lowe NJ, Duvic M, Friedman DJ, Jegasothy BV, Jorizzo JL, Shmunes E, Tschen EH, Lew Kaya DA, Lue JC, Sefton J, Gibson JR, Chandraratna RA. 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.

3. Weinstein GD. Tazarotene gel: efficacy and safety in plaque psoriasis. J Am Acad Dermatol 1997; 37: S33-8.

4. Marks R. Clinical safety of tazarotene in the treatment of plaque psoriasis. J Am Acad Dermatol 1997; 37: S25-32.

5. Chandraratna RA. Tazarotene: the first receptor-selective topical retinoid for the treatment of psoriasis. J Am Acad Dermatol 1997; 37: S12-7.

AUTHORS' ADDRESSES

Giuseppe Stinco, MD, dermatologist, Institute of Dermatology, D.P.M.S.C., University of Udine, Gemona Hospital, 33013 Gemona del Friuli (Udine), Italy
Giovanni Bragadin, MD, same address
Vincenzo De Francesco, MD, dermatologist, same address
Alfonsina Frattasio, MD, dermatologist, same address
Pasquale Patrone, MD, professor of dermatology, Head of Institute, same address