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Original article

Clinical evaluation of topical tacalcitol efficacy in extending the remission period between nb-UVB phototherapy cycles in psoriatic patients

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Abstract. Psoriasis is a very common dermatological disease affecting a large part of the world population. In its most common form, psoriasis vulgaris, many topical drugs are available to treat the localized forms, and the recurrence of the dermatosis. Among topicals, tacalcitol has been proven to be effective and devoid of side effects which are typical of Vitamin-D3 analogues or derivates. The aim of this retrospective study was to evaluate the efficacy of topical tacalcitol vs calcipotriol and emollient treatment of the first recurring lesion in order to induce a longer remission period before the retreatment with nb-UVB phototherapy in a population of 90 psoriatic patients. In this trial, the time between the first relapsing plaque appearance and retreatment with nb-UVB resulted in 25, 16 and 11 days for tacalcitol, calcipotriol and emollient respectively, with a statistically significant difference for tacalcitol ($p<0.0001$). These results proved that tacalcitol treatment is effective in increasing the time interval in consecutive phototherapy cycles and in reducing the total amount of UV exposure. (www.actabiomedica.it)

Key words: Psoriasis, tacalcitol, phototherapy

Introduction

Psoriasis is a very common, chronic and recurrent dermatological disease affecting a wide range of people; it is estimated that almost 2% of the world population is affected (1). The typical skin lesions are erythematous, scaly patches or plaques of varying size with a classical localization on the elbows, knees, lumbo-sacral region and the scalp. Normally, from these primitive localizations, the lesions tend to widespread to more extended areas of the body. Psoriasis has the tendency to recurr after treatment discontinuation, and the disease-free period (the time interval between disease recurrences) becomes shorter and shorter if an effective therapy is not performed as soon as possible (2). The most common form of disease is the so-called psoriasis vulgaris, also known as the chronic-plaque type which, at histopathologic examination, is characterized by an inflammatory infiltrate, various vascular changes in the dermal layer, and epidermal hyperproliferation (3).

A topical treatment for psoriasis is mandatory, due to the fact that it is the elective treatment in localized forms, in single large plaques, or when the lesions do not exceed 20% of body surface area. Moreover, the local treatment may be very helpful in integrating systemic treatment in recalcitrant forms. Topical treatments such as emollients, keratolytics, tar, dithranol, corticosteroids and vitamin-D derivatives are all used in order to improve scaliness, inflammation, and to reduce the pool of cytokines and growth factors which play a key role in promoting inflammation and hyperproliferation of the epidermis (4). The continuous use of these topical drugs is also crucial

since it stimulates the tendency of taking care of one's health, and improves the psychological attitude towards the illness and the self-consciousness of the disease (5).

Among these drugs, the Vitamin D3 analogue, tacalcitol, has proven to be an effective drug in the topical treatment of psoriasis (6); it is also particularly well tolerated since the onset of side effects such as local irritation, burning and pruriginous sensations are seldom reported in the literature (6).

The spreading of psoriasis to wider areas of the body makes other types of treatments mandatory (body surface area – BSA – ≥ 20%). An important treatment, in responsive patients, is phototherapy. Unlike in the past, in which PUVA therapy was widely prescribed to psoriatic patients, UVB has proven to be effective with lower side effects and longer-lasting efficacy (7). Narrow band UVB (nb-UVB) in particular, is more selective in treating psoriasis and its therapeutical and biological mechanisms are well known to dermatologists (8). Most of the responding psoriatic patients who undergo periodical nb-UVB treatments, after achieving a total or partial remission of the clinical lesions, need to undergo a period of treatment discontinuation. During this period, in most patients a recurrence of a psoriatic plaque is observed; usually this single plaque tends to recur in the same body area (Table 1).

The objective of the present study was to assess the efficacy of tacalcitol vs calcipotriol and emollients in the treatment of these relapsing plaques in order to extend the phototherapy suspension period.

Methods

Among the patient population attending the Physiotherapy Unit of our Department of Dermatological Sciences, University of Florence, in the period between January 2007-January 2008, a total of 90 outpatients, 48 males and 42 females were selected and included in this retrospective study.

Table 1. Site of lesion relapse in the patients evaluated in the study

No. Patients (%)	Site of lesion relapse
36 (40)	Anterior Tibial Area
21 (23.3)	Elbow
15 (16.6)	Knee
15 (16.6)	Scalp
3 (3.3)	Perianal area

The evaluation was performed in patients that were periodically treated with nb-UVB for a total number of months listed in tables 1-4 (with a suitable number of intervals between the phototherapic cycles). All of them were affected by psoriasis vulgaris covering more than 20% of the body surface at the beginning of the phototherapic treatment, which was discontinued when clinical remission was achieved (PASI score < 2).

During the suspension period, the patients received one of the three following treatments: tacalcitol ointment or emulsion (30 patients); calcipotriol cream or solution (30 patients); emollient galenic formulation (30 patients) composed of sweet almond oil 30% and white petrolatum 70%. Patients were treated as soon as the relapsing plaque appeared. The choice of the formulation (ointment/cream vs. emulsion/solution) was based on the site of occurrence of the lesion (hairy vs non-hairy vs folds).

Baseline patient characteristics of the treatment groups were compared using one-way analysis of variance.

The primary efficacy parameter was the number of days from the start of relapsing plaque treatment to the start of retreatment with nb-UVB. Treatments were compared using one-way analysis of variance. When the treatment effectiveness was significant at level of 0.05, multiple comparisons were performed, adjusting p-value by the Tukey method.

Results

The comparison of baseline patient characteristics showed no statistically significant difference among groups, including the total amount of UVB exposure in months (34.6, 35.2 and 35.8 for tacalcitol, calcipotriol and emollient group respectively) (Table 5). None of the patients reported local intolerance or systemic side-effects.

The mean time from the start of relapsing plaque treatment to the start of retreatment with nb-UVB is

Table 2. Tacalcitol

Patients	Age	Duration of cumulative nb-UVB treatment (Months)	Time before first relapsing plaque appearance (days)	Time before retreatment with nb-UVB is necessary (days)*	Site of Lesion Relapse
M[a]-1	32	31	20	21	Knee
M-2	36	39	15	21	Anterior tibial area
M-3	40	42	10	27	Elbow
M-4	52	34	40	28	Scalp
M-5	30	38	22	23	Anterior tibial area
M-6	47	37	21	24	Anterior tibial area
M-7	49	35	30	20	Elbow
M-8	34	36	32	25	Anterior tibial area
M-9	55	25	36	25	Perianal area
M-10	40	29	37	26	Anterior tibial area
M-11	58	33	42	30	Knee
M-12	44	42	60	21	Elbow
M-13	39	44	22	27	Elbow
M-14	52	36	12	29	Anterior tibial area
M-15	36	38	11	28	Scalp
M-16	53	19	10	31	Knee
F[b]-1	34	39	20	28	Elbow
F-2	39	30	36	25	Elbow
F-3	54	41	43	21	Anterior tibial area
F-4	47	40	66	23	Elbow
F-5	52	38	30	24	Anterior tibial area
F-6	36	32	31	24	Scalp
F-7	55	28	25	27	Anterior tibial area
F-8	38	35	27	20	Knee
F-9	31	33	30	21	Anterior tibial area
F-10	48	36	27	21	Scalp
F-11	34	39	28	28	Knee
F-12	43	47	31	26	Anterior tibial area
F-13	54	18	17	27	Scalp
F-14	51	26	18	30	Anterior tibial area

* Time (days) of duration of topical treatment alone after appearance of the first recurrent plaque and before a new nb-UVB cycle
[a]M: Male; [b]F: Female

reported in figure 1. The mean number of days before the retreatment was 25 for the tacalcitol group and, 16 and 11 days for calcipotriol and emollient group respectively, showing a highly significant difference in favour of the tacalcitol treatment ($p < 0.0001$).

Conclusions

Psoriasis is a common dermatological disease which is not always easy to treat. The most common form, psoriasis vulgaris, is normally treated with many different topical drugs in order to achieve a clinical remission of the lesions and a better quality of life. When psoriasis vulgaris interests a body surface area (BSA) ≥ 20%, cycles of nb-UVB prove to be effective (8-10), but, even in patients who respond well to phototherapy, a recurrence always takes place.

The aim of our study was to recognise and isolate the first clinical recurring lesion and to treat it with a topical formulation, in order to postpone, as long as possible, a new phototerapic treatment, considering the photocarginogenic risks of phototherapy (11). A variety of topical treatments are available on the market and, in

Table 3. Calcipotriol

Patients	Age	Duration of cumulative nb-UVB treatment (Months)	Time before first relapsing plaque appearance (days)	Time before retreatment with nb-UVB is necessary (days)*	Site of Lesion Relapse
M[a]-1	57	20	25	15	Scalp
M-2	36	25	12	17	Knee
M-3	49	19	13	16	Elbow
M-4	31	38	14	14	Anterior tibial area
M-5	38	46	32	15	Anterior tibial area
M-6	50	44	50	16	Anterior tibial area
M-7	52	32	60	14	Elbow
M-8	41	37	71	24	Anterior tibial area
M-9	30	43	33	18	Scalp
M-10	47	35	11	12	Anterior tibial area
M-11	39	29	10	15	Knee
M-12	53	38	8	17	Anterior tibial area
M-13	58	40	21	18	Elbow
M-14	36	36	24	18	Scalp
M-15	43	36	27	17	Perianal area
M-16	31	42	32	12	Scalp
F[b]-1	54	37	32	21	Elbow
F-2	40	33	33	22	Anterior tibial area
F-3	40	28	34	14	Knee
F-4	36	32	40	17	Elbow
F-5	52	42	25	14	Anterior tibial area
F-6	31	39	26	16	Knee
F-7	38	31	26	16	Anterior tibial area
F-8	45	48	31	20	Elbow
F-9	44	20	13	11	Scalp
F-10	57	38	15	12	Anterior tibial area
F-11	51	37	49	20	Elbow
F-12	33	36	14	14	Anterior tibial area
F-13	30	40	22	12	Knee
F-14	58	35	16	14	Anterior tibial area

* Time (days) of duration of topical treatment alone after appearance of the first recurrent plaque and before a new nb-UVB cycle
[a]M: Male; [b]F: Female

this study, the efficacy of two synthetic analogues of Vitamin D3 (tacalcitol and calcipotriol) and an emollient were analysed. The result showed that tacalcitol consistently increased the time interval between disease recurrencies with respect to the other products.

There are many reports in the literature (12, 13) proving the clinical efficacy and the safety profile of tacalcitol. Tacalcitol is a synthetic Vitamin D3 analogue; it is able to modulate the growth of the epidermal layer and to reduce the inflammatory response linking an intracellular receptor, the VDR receptor (14). The VDR receptor belongs to the family of steroid receptors and is normally expressed by both keratinocytes and fibroblasts.

Calcipotriol is the active metabolite of Vitamin D3; it has many functional properties with tacalcitol, showing affinity with the same receptor VDR but at a lower extent than tacalcitol, and is therefore less effective in reducing keratinocytes proliferation and differentiation (4, 12, 15). The influence of tacalcitol on the phosphocalcine metabolism is however markedly lower than that of calcipotriol, thus tacalcitol is much safer because it is not involved in the regulation of phosphorus and calcium levels in plasma (12). More-

Table 4. Emollient

Patients	Age	Duration of cumulative nb-UVB treatment (Months)	Time before first relapsing plaque appearance (days)	Time before retreatment with nb-UVB is necessary (days)*	Site of Lesion Relapse
M[a]-1	32	20	20	8	Anterior tibial area
M-2	55	41	21	7	Elbow
M-3	45	39	21	8	Knee
M-4	53	33	50	14	Scalp
M-5	42	40	52	13	Anterior tibial area
M-6	58	48	30	10	Elbow
M-7	36	36	31	10	Knee
M-8	39	29	21	12	Anterior tibial area
M-9	43	39	29	15	Anterior tibial area
M-10	47	31	28	10	Anterior tibial area
M-11	51	39	27	13	Knee
M-12	45	41	50	10	Elbow
M-13	50	25	40	12	Scalp
M-14	58	52	20	12	Anterior tibial area
M-15	39	38	21	10	Elbow
M-16	33	41	32	12	Anterior tibial area
F[b]-1	30	18	29	10	Scalp
F-2	55	35	20	11	Anterior tibial area
F-3	49	37	19	6	Knee
F-4	43	39	15	12	Elbow
F-5	37	32	17	6	Scalp
F-6	32	24	18	8	Perianal area
F-7	55	60	40	19	Anterior tibial area
F-8	54	39	33	14	Elbow
F-9	51	55	50	12	Knee
F-10	45	48	62	14	Anterior tibial area
F-11	50	44	43	15	Anterior tibial area
F-12	31	14	23	10	Anterior tibial area
F-13	34	18	28	7	Elbow
F-14	33	19	27	11	Scalp

* Time (days) of duration of topical treatment alone after appearance of the first recurrent plaque and before a new nb-UVB cycle
[a] M: Male; [b] F: Female

Table 5. Total amount of UVB exposure (months) for the patients evaluated in the study

Treatment	No. Patients	Mean Age (SD)	Mean Duration of Cumulative nb-UVB Treatment in Months (SD)
Tacalcitol	30	43.77 (8.59)	34.67 (6.78)
Calcipotriol	30	43.33 (9.28)	35.20 (7.36)
Emollient	30	44.17 (8.92)	35.80 (11.34)

over, a tacalcitol peculiarity is that it inhibits the expression of RNA messenger for the c-fos and c-myc genes; both genes code for the nuclear DNA-binding proteins that are implicated in cellular proliferation (16). Moreover, tacalcitol is able to reduce the synthesis of some cytoskeleton proteins such as cytokeratin-16 and vimentin, that are normally overexpressed in psoriatic skin (16).

This trial showed that tacalcitol ointment/emulsion is more effective than calcipotriol and emollients in maintaining clinical remission between consecutive phototherapy cycles, obtaining a longer disease-free period before retreatment becomes necessary. This is very important since it reduces the nb-UVB phototherapy cycles and side effects related to chronic UV-exposure, increasing patients' overall quality of

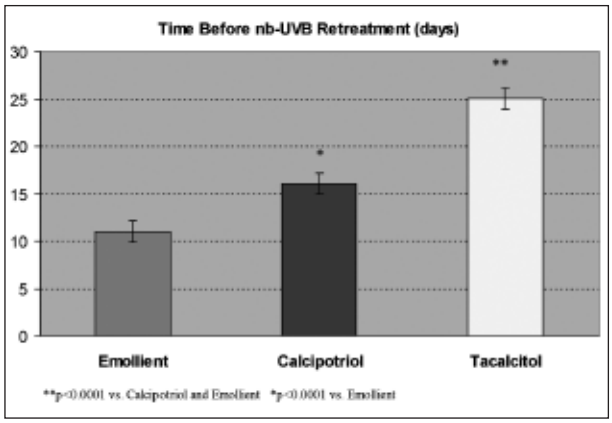

Figure 1. Comparison of the different topical treatments in terms of disease-free days

life, giving them the possibility to perform their own therapy at home once a day.

It is also interesting to consider the numerous clinical studies that showed an increase in the efficacy of PUVA or nb-UVB therapies when combined with once-daily applications of topical tacalcitol, resulting in a significant reduction of the total dose of radiations (17, 18).

In summary, tacalcitol may be particularly useful in reducing the possible long-term hazards of chronic UV exposure working in a double way, decreasing the length of a single cycle and decreasing the number of cycles /year.

References

1. Langley RG, Krueger GG, Griffiths CE. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis* 2005; 64 Suppl 2: 18-23.
2. Krueger GG, Bergstresser PR, Lowe NJ, Vorheers JJ, Winstein GD. Psoriasis. *J Am Acad Dermatol* 1984; 11: 937-47.
3. Krueger JG, Bowcock A. Psoriasis pathophysiology: current concepts of pathogenesis. *Ann Rheum Dis* 2005; 174: 2005; 64: ii30-ii36.
4. Mason J, Mason AR, Cork MJ. Topical preparationas for the treatment of psoriasis : a systemic review. *British J Dermatol* 2002; 146: 351-64e.
5. Urpe M, Pallanti S, Lotti T. Psychosomatic factors in dermatology. *Dermatol Clin* 2005; 23 (4): 601-8.
6. Kragballe K. The use of vitamin D analogues in dermatology. *Curr Opin Dermatol* 1995; 16: 198: 203.
7. Honigsmann H. Phototherapy for psoriasis. *Clin Exp Dermatol* 2001; 26: 34e3-350.
8. Kirke SM, Lowder S, Lloyd JJ, Diffey BL, Matthews JN, Farr PM. A randomized comparison of selective bradband UVB and narrowband UVB in the treatment of psoriasis. *J Invest Dermatol* 2007; 127 (7): 1570-1.
9. Dawe RS, Rainwright NJ, Cameronm H, et al. Narrowband ultraviolet B phototherapy for chronic plaque psoriasis: three times or five times weekly treatment. *Br J Dermatol* 1998; 138: 833-9.
10. Yuehua Y, Khalaf AT, Xiaoxiang Z, Xinggang W. Narrowband ultraviolet B and conventional UVB phototherapy in psoriasis: a randomised controlled trial. *Am J Applied Sciences* 2008; 5 (8): 905-8.
11. Man I, Crombie IK, Dawe RS, Ibbotson SH, Ferguson J. The photocarcinogenic risk of narrowband UVB (TL-O1) phototherapy: early follow-up data. *Br J Dermatol* 2004; 151: 289-97.
12. Leone G, Pacifico A. Profile of clinical efficacy and safety of topical tacalcitol. *Acta Bio Med* 2005; 76: 13-9.
13. Lecha M, Mirada A, Lopez S, Artes M. Tacalcitol in the treatment of psoriasis vulgaris: the Spanish experience. *J Eur Acad Dermatol Venereol* 2005; 19 (4e): 414-7.
14. Van de Kerkhof PC. An update on Vitamin D3 analogues in the treatment of psoriasis. *Skin Pharmacol Appl Skin Physiol* 1998; 11: 2-10.
15. Nishimura M, Hori Y, Nishiama S, Nakamizo Y. Topical 1a,24(R)-dihydroxyvitamin D3, for the treatment of psoriasis. Review of the literature. *Eur J Dermatol* 1993; 3: 255-61.
16. Kobayashi H, Fukaya T, Ogiso Y, et al. Vitamin D3 inhibits the mRNA expressions of fos and myc oncogenes in organ cultured skin. *J Invest Dermatol* 1991; 96: 616.
17. Kokelj F, Plozzer C, Guadagnino A. Topical tacalcitol reduces the total UVB dosage in the treatment of psoriasis vulgaris. *J Dermatol Treat* 1996; 7: 265-6
18. Messer G, Degitz K, Plewig G, Rocken M. Pretreatment of psoriasis with the vitamin D3 derivative tacalcitol increases the responsiveness to 311-nm ultraviolet B: results of a controlled, right-left study. *Br J Dermatol* 2001; 144: 628-50.

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