UVB phototherapeutic modalities. Comparison of two treatments for chronic plaque psoriasis

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ABSTRACT

Background: Combination UVB phototherapeutic regimens were introduced to improve therapeutic results and reduce cumulative UVB doses.
Objective. Broadband UVB and UVB + bergamot oil (UVBB) therapies in the treatment of psoriasis were compared with regard to: efficacy, side effects, mean number of procedures, mean UVB dose, and duration of remissions.
Patients/methods. One hundred and ninety three (193) patients randomly divided into two groups were treated: Group I with UVB monotherapy and Group II with UVB and bergamot oil (UVBB).
Results. Overall assessment of the efficacy of the two treatment regimens demonstrated no statistically significant differences in either the post-therapy PASI values (t = 0.27, p = 0.786) or the duration of remissions (t = 0.22, p = 0.904). However, significant differences in the number of procedures (t = 2.3, p = 0.04) and the cumulative UVB doses were established (t = 3.4, p = 0.004).
Conclusion. UVBB phototherapy significantly reduces the UVB doses and the duration of treatment for psoriatic patients.

KEY WORDS

psoriasis, UVB, bergamot oil

Introduction

Psoriasis is a common chronic and relapsing dermatosis that affects between 1% and 3% of the world's population. Recent studies have demonstrated that it may be assigned to the group of inflammatory, T-cell mediated dermatoses (1). Increased epidermal turnover and keratinocyte hyperproliferation accompanied by vascular proliferation with associated inflammation are characteristic (2, 3). The role of T-cells was demonstrated by remissions achieved after treatment of psoriatic patients with a drug containing diphtheria toxin and the receptor-binding domain of IL-2, which are both toxic to activated T-cells (4). Application of IL-10 targeting T-cells and monocytes also leads to significant clinical improvement represented by reduction of the Psoriasis Area and Severity Index (PASI) (5, 6). Despite the obvious progress achieved in clarifying the etiopathogenesis of the disease, its treatment still remains a challenge: various therapeutic modalities are applied

with all of them leading to remissions of varying duration, but not inducing a definite cure.

Phototherapy is still a mainstay in the treatment of the disease. Ultraviolet B (UVB) and psoralen + UVA (PUVA) reduce the number of activated T-cells in psoriatic skin by inducing T-cell apoptosis (7–9). One main concern associated with phototherapy is the development of long-term side effects: photoaging and photocarcinogenesis. One of the main challenges for dermatologists is to reduce the cumulative UV doses. This can be achieved by improvement of the phototherapeutic devices (10), application of combination regimens (11–12), or performing rotational therapy (13).

The aim of the present study was to assess the efficacy and side effects of broadband-UVB as compared to UVB + topical photosensitizer bergamot oil (UVBB) in the treatment of chronic plaque psoriasis.

Materials and methods

One hundred and ninety three (193) patients were treated. The characteristics of the study population are presented in Table 1. The only inclusion criterion for the patients was plaque-type psoriasis. Exclusion criteria were: hyper-sensitivity to sunlight; use of phototoxic, photosensitizing, or immunosuppressive drugs; serious neurological or heart diseases or concomitant infectious diseases.

The patients were randomly assigned as they visited the phototherapeutic center: the first patient to Group I, the second to Group II, and so on:

Group I (n = 102) patients were treated with UVB monotherapy;

Group II (n = 91) patients were treated with UVB and a topical photosensitizer, bergamot oil (UVBB) (14, 15).

The Psoriasis Area and Severity Index (PASI) (16) was used to evaluate clinical condition. This was assessed at the start and at the end of therapy by the same investigator (S. Valkova).

The equipment used in both groups was a Waldmann 7001K whole-body cubicle (Waldmann Medizintechnik, Villingen-Schwenningen, Germany) equipped with 26 UVA lamps (Waldmann F85/100W PUVA) with peak emission of 365 nm and 13 UVB lamps (Waldmann F85/100W PUVA-UV 21) with peak emission of 310–315 nm.

The initial UVB dose was determined according to phototype: 0.04 J/cm^2 for phototype II and 0.05–0.06 J/cm^2 for phototypes III and IV. This was increased by 0.02 J/cm^2 every second procedure if there was no preceding erythema, itching, or pain. When there were such complaints, the dose administered in the next session remained the same or the patients missed 1–2 procedures until the side effects subsided. The initial UVB dose and its rate of increase were the same for Group II.

Patients in Group II applied bergamot oil on the psoriatic plaques 30 min before the procedures. Sessions were held three times weekly (on Mondays, Wednesdays, and Fridays) in both groups. Before starting treatment, all patients used keratolytic agents (10% salicylic acid in W/O emulsion and 10% urea in O/W emulsion) to remove the psoriatic scales. During the therapeutic course they applied only emollients in unlimited quantities. The treatment was either conducted until complete clearing, or discontinued if there was no significant improvement after 5 consecutive procedures.

The Statgraphics Plus for Windows 5.0 (Manugistic Inc., Rockville, Maryland, USA) program was used for statistical analysis based on Student's t-test. Data are given as mean ± SE.

Results

Group I (UVB monotherapy)

A statistically significant difference was established between PASI values before (8.9 ± 0.3) and after (1.1 ± 0.1) therapy (t = 30.9, p = 0.001). The first signs of improvement appeared after 3 or 4 procedures. The minimum number of sessions necessary for recovery was 12 and the maximum 22. Clinical recovery of patients with more severe forms of psoriasis required higher UVB doses and a greater number of procedures.

In 73 (72%) of the 102 patients treated, the duration of the remissions was followed. The appearance of erythema and scaling spreading on more than 5% of the body surface was considered to be a relapse of the disease. The maximum duration of remissions was 12 months and the minimum was 2 months. The shortest remissions were observed in patients with the most severe forms of the disease.

Forty-three (42%) of the 102 patients underwent a second phototherapeutic course after the occurrence of a relapse. Statistical analysis revealed no significant difference between PASI values before the first (mean 8.9 ± 0.3) and the second (mean 9.0 ± 0.8) courses (t = 0.12, p = 0.560). This also applied to the mean UVB doses and the number of procedures necessary for recovery (UVB dose: course I: 3.1 ± 0.2 J/cm^2; course II: 3.4 ± 0.4 J/cm^2; t = 0.92, p = 0.654; number of procedures: course I: 15.6 ± 0.5; course II: 16.2 ± 0.4; t = 0.84, p = 0.248).

Side effects during UVB monotherapy appeared in 48 patients (47%) and included erythema in 19 (28%), itching in 3 (4%), skin dryness in 40 (59%), non-specific rash in 4 (6%), and herpes labialis in 2 (3%).

Table 1. Characteristics of the study population: sex, age, phototype and duration of psoriasis.

Group	Sex		Age (years)	Phototype			Disease duration (years)
	Male	Female		II	III	IV	
I UVB monotherapy (*n* = 102)	65 (64%)	37 (36%)	17–70 (mean 40.3 ± 1.2)	22 (22%)	74 (73%)	6 (5%)	0.5–32 (mean 10.3 ± 0.7)
II UVBB therapy (*n* = 91)	54 (59%)	37 (41%)	18–63 (mean 41.5 ± 2.3)	23 (25%)	63 (69%)	5 (6%)	2–62 (mean 10.3 ± 1.1)
Total (*n* = 193)	119	74	mean 40.9 ± 0.9	45	137	11	mean 11.9 ± 0.6

Table 2. Mean PASI score, cumulative UVB dose, number of exposures and duration of remissions in patients with psoriasis treated with UVB and UVBB phototherapeutic modalities.

Phototherapeutic regimen	Mean			
	PASI* after treatment	UVB dose (J/cm²)	Number of exposures	Duration of remissions (months)
UVB monotherapy (*n* = 102)	1.1 ± 0.1	3.8 ± 0.2	15.9 ± 0.4	6.8 ± 0.3 (*n* = 73)
UVB+ topical photosensitizer (*n* = 91)	0.8 ± 0.2	2.9 ± 0.2	14.8 ± 0.7	7.3 ± 0.8 (*n* = 53)
Statistics	*t* = 0.27 *p* = 0.786	*t* = 3.4 *p* = 0.004	*t* = 2.3 *p* = 0.04	*t* = 0.22 *p* = 0.904

** Psoriasis Area and Severity Index (10)*

Group II (UVBB therapy)

A statistically significant difference was established between PASI values before (10.3 ± 0.7) and after (0.8 ± 0.2) therapy (t = 15.01, p = 0.001). The first signs of improvement appeared after 2 to 3 procedures. The minimum number of sessions necessary for clinical recovery was 10 and the maximum was 17. The treatment of patients with more severe forms of psoriasis required higher UVB doses and a greater number of procedures.

In 53 (58%) of the 91 patients treated the achieved remissions were followed. The maximum remissions lasted 11 months and the minimum 2 months. Side effects were observed in 34 (37%) and included erythema in 15 (44%), itching in 10 (29%), burning and pain in 8 (24%), and herpes labialis in 1. Hyperpigmentation of the psoriatic plaques was observed in all patients at the end of the therapeutic course.

Overall assessment of the efficacy of the two treatment regimens demonstrated no statistically significant difference in either the PASI values after therapy or the duration of remissions (Table 2). There was, however, a significant difference in the number of sessions and the UVB dose necessary for recovery (Table 2). They were lower for the combination regimen.

Discussion

Despite their favorable therapeutic efficacy, UV rays cause various acute (erythema, burning) and late (photoaging, photocarcinogenesis) side effects (17, 18). In this respect, a number of combination phototherapeutic regimens have been introduced, all of them aiming at improving therapeutic results, reducing the cumulative UVB doses and duration of treatment, and prolonging the remissions.

The efficacy of UVB monotherapy in psoriasis has been demonstrated in a number of investigations (10, 19, 20) and was confirmed in our first group of 102 patients by reaching a final PASI = 0 in 48 of them. The inability to achieve PASI = 0 in all patients is due to the limited effect of the rays on the scalp. The lower extremities and the more severe forms of psoriasis were also more resistant to therapy.

The duration of remissions achieved in our patients after UVB monotherapy is very similar to results reported by other authors even after PUVA (11, 21, 22). This may be due to the favorable climatic conditions in Bulgaria, which are suitable for thalassotherapy, and to the fact that many patients use such treatment from June to September.

Our observations (unpublished data) of the effect

of systemic and/or local corticosteroids on psoriasis demonstrate that their use leads to shorter remissions and sometimes even to more severe relapses. The results of this study allow us to conclude that UVB phototherapy does not induce more intense relapses and that subsequent courses require neither higher UVB doses nor a greater number of procedures.

Bergamot oil is a natural photosensitizer isolated from the bergamot orange (*Citrus bergamia*). The extract from bergamot peels contains coumarins and furocoumarins: 5-methoxypsoralen (5-MOP) or bergapten, 5,7 dimethoxycoumarin (citropten), 5-geranoxypsoralen (bergamottin), 5-geranoxy-7-methoxycoumarin, etc. (14, 15). The photosensitization to material contained in bergamot oil is mainly attributed to 5-MOP (15). It is known that psoralens (furocoumarin isomers) are successfully applied in local and systemic PUVA treatments of psoriasis. There is also data for the association of psoralens with UVB rays (23, 24). We tried to enhance the therapeutic efficacy of UVB monotherapy with topical application of bergamot oil. To our knowledge, no such combination has been mentioned in the literature. Surprisingly, this UVBB regimen did not lead to better clinical results compared to UVB monotherapy. This could be explained by the fact that the action spectrum of psoralens is mainly in the UVA range. Another reason could be the strong pigmentogenic activity of 5-MOP. Pigmentation is a limiting factor as it increases the tolerance of the skin to UV irradiation.

The limitations of this study are related both to the biases associated with determining PASI values and the fact that the person assessing them was familiar with the type of treatment administered. However it is not likely that this significantly influenced the results because the criteria for estimating the PASI index are well defined and in all patients the index was assessed by the same dermatologist. This was confirmed by the fact that UVBB therapy did not lead to better clinical results, which was not expected.

In conclusion, our observations demonstrate that the use of combination phototherapeutic regimens significantly reduces UVB doses and duration of treatment for psoriatic patients. Nowadays, narrowband UVB treatment (UVB 311 nm) (25) is becoming increasingly popular. An analogous study based on UVB 311 nm could be an opportunity to develop new combination phototherapeutic methods for the treatment of psoriasis.

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