

The efficacy of PUVA and UVB 311 nm in small plaque parapsoriasis

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ABSTRACT

Introduction. Small plaque parapsoriasis (SPP), a disease with a characteristic clinical presentation, was for many years regarded as belonging to the group of cutaneous lymphomas. At present, it is no longer considered a precursor of mycosis fungoides. Although lesions may resolve spontaneously in response to sun exposure, the condition can be improved with topical corticosteroid therapy but, primarily, with various forms of phototherapy.

Objective. To compare the efficacy of two SPP treatment modalities: UVB 311 nm irradiation and PUVA.

Material and methods. The study was conducted in 88 consecutive patients with histopathologically verified diagnosis of SPP who were treated in the Dermatology Department in Warsaw between 2001 and 2013. UVB 311 nm phototherapy (TL-01 lamps) was administered to a total of 53 patients (21 women and 32 men). PUVA therapy involving oral psoralens was given to 35 patients (13 women and 22 men).

Results. Complete regression of skin lesions was achieved in all the patients. The mean duration of UVB 311 nm phototherapy was 10 weeks, which was equivalent to the mean UV dose of 22 J/cm². The mean duration of PUVA treatment was 7 weeks (43.6 J/cm²). Relapse of the disease occurred in 60.3% of patients treated with UVB 311 nm irradiation after an average of 12.2 months. In the PUVA group, relapse was observed in 60% of the study patients after an average of 13.8 months.

Conclusions. The study provided evidence for the high efficacy of UVB 311 nm irradiation, which was shown to be comparable to the efficacy of PUVA. Considering the chronic and recurrent nature of the disease, which necessitates multiple courses of treatment, UVB 311 nm should be recommended as a treatment of choice for SPP.

INTRODUCTION

The term parapsoriasis was first introduced into medical nomenclature by L.A.J. Brocq in the early 20th century. Brocq claimed that due to the resemblance of skin eruptions to psoriasis the term parapsoriasis can be used to characterize a range of previously unde-

scribed skin conditions of similar morphology and uncertain aetiology. The first classification of parapsoriasis included: *pityriasis lichenoides chronica*, *pityriasis lichenoides et varioliformis acuta*, *parapsoriasis en plaque – small plaque and large plaque* [based on 1].

Skin lesions occurring in *small plaque parapsoriasis* (SPP) are quite distinctive. They are patches with diam-

eters ranging from 2 cm to 5 cm, or larger (up to 10 cm), pale pink in colour, arranged in a linear or oblong pattern, occasionally resembling fingerprint marks on the skin. The morphology of skin lesions is usually homogeneous, and the patches are superficial. In fact, their ephemeral and fleeting nature is often emphasized. The most noticeable feature of clinical presentation is the symmetry of skin lesions. They are located primarily along the sides of the trunk and on the flexor aspects of upper and lower extremities. The head is not usually affected. Deviations from the general rule are sometimes observed, with lesions localized on the lower legs, or in the inguinal, axillary and scapular regions. As a rule, no signs of atrophy, infiltration or poikiloderma appear, though when the condition is severe, reddish or yellow-brown oedematous-erythematous plaques may emerge (hence the old term: *xanthoerythroderma perstans*). There may also be skin eruptions featuring small irregular markings on the surface (pseudolichenification) – or cutaneous thinning which gives the skin a tissue-paper-like appearance (pseudoa-trophy). Skin lesions are not accompanied by any general complaints. There is no lymph nodes enlargement at any stage of the disease. A certain group of patients, however, report skin itching of varying intensity. Skin lesions commonly develop seasonally, peaking in autumn and winter, and may resolve spontaneously under the influence of sun exposure in summer [2, 3]. In the absence of definite symptoms, patients often choose not to see their doctor or delay an appointment until after multiple relapses of the disease.

The diagnostic process should incorporate clinical and histopathological findings. The differential diagnosis should include *large plaque parapsoriasis* – LPP, *dermatitis seborrhoica*, *eczema nummulare*, *granuloma annulare*, *pityriasis versicolor* and – above all – *mycosis fungoides* (MF) (of erythematous stage). In the latter case, clinical evaluation must be definitely supported by histopathology. The histopathological manifestations of SPP usually involve non-specific inflammation, signs of epidermotropism, focal parakeratosis or acanthosis. In the event of significant uncertainty, immunohistochemical testing is necessary to determine the phenotype of infiltrating lymphocytes [2, 3].

The currently dominant view is that SPP, as opposed to LPP, has no potential of transformation into MF [2–4], though there are isolated reports on such cases in medical literature [5, 6]. Finnish authors [5] have retrospectively analyzed a total of 69 patients with SPP and 36 patients with LPP followed up for a period of 25 years. Based on that material, cancerous transformation into *mycosis fungoides* was confirmed not only in 12 (33%) of patients with LPP but also in 7 (10%) patients with SPP. Belousova *et al.* [6] described the case of a patient whose SPP-specific features persisted for three years before developing into larger foci, partially

infiltrative in nature, revealing histopathological and immunohistochemical aberrations typical for *mycosis fungoides*. In the remaining group of 27 patients with SPP, who were followed up by the authors for 1.2 to 52 years (mean of 10 years), SPP was not found to have progressed into MF. It seems that the main reasons for concern are increasing itch, increasingly shorter periods of remission and, in particular, emergence of infiltrative lesions. Selection of the method of SPP treatment depends on the extent of cutaneous lesions, the frequency of relapses and the presence of itch. Although topical corticosteroids are sometimes prescribed, the basic therapeutic modality is UV irradiation treatment. Available techniques include broadband UVB, narrow-band UVB (UVB 311 nm), UVA1 and PUVA.

OBJECTIVE

The aim of the study was to compare the efficacy and long-term effects of SPP treatment with PUVA and UVB 311 nm phototherapy.

MATERIAL AND METHODS

The study involved 88 patients including 34 women (38.6%) and 54 men (61.4%) who visited the Outpatient Clinic of the Dermatology Department (Medical University of Warsaw) in 2001–2013. The diagnosis of small plaque parapsoriasis was based on clinical manifestations and histopathological examination (performed in all the study patients). The earliest onset of SPP skin lesions was in 1987 and the latest – 4 months before the medical appointment. In the majority of patients cutaneous lesions were arranged in a typical symmetrical pattern on the flexor aspects of upper and lower extremities, on the sides of the trunk and thighs. They appeared as oval or round patches, 2–10 cm in diameter. All the patients had quite extensive skin involvement: 5–20 lesions were identified in 20 patients, 20–50 lesions in 58 patients and over 50 lesions – in 20 patients. There were no significant differences in the extent of skin lesions between the groups treated with UVB 311 nm and PUVA. A total of 47 patients had previously been treated with PUVA or UVB 311 nm phototherapy. The general characteristics of patients assigned to different therapeutic modalities are listed in tables I and II.

UVB 311 nm irradiation was performed in a cabin with TL-01 lamps, three times a week, with the starting dose of 0.2 J/cm². The dose was subsequently increased by 0.1 J/cm² every other treatment. PUVA was applied after oral administration of 8-methoxypsoralen (0.5–0.6 mg/kg BW, 1 h before UVA exposure). The treatments were performed in a cabin equipped with standard UVA 320–400 nm lamps

Table I. Characteristics of patients irradiated with UVB 311 nm

Gender	Age [years]			Duration of the disease [months]			Extent of skin lesions	
	Mean	SD	Scatter	Mean	SD	Scatter	Number of lesions	Number of patients
F = 21 (40%)	65.2	13.9	28–88	42.8	36.5	3–120	5–20	12
M = 32 (60%)	58.1	13.2	30–77	53.5	44.5	3–180	20–50	35
Σ = 53	60.9	13.8	28–88	49.3	41.5	3–180	> 50	6

Table II. Characteristics of patients treated with PUVA

Gender	Age [years]			Duration of the disease [months]			Extent of skin lesions	
	Mean	SD	Scatter	Mean	SD	Scatter	Number of lesions	Number of patients
F = 13 (37.2%)	60.9	17.8	26–81	34.1	30.0	6–120	5–20	8
M = 22 (62.8%)	55.0	13.0	33–75	38.6	40.5	1–180	20–50	23
Σ = 35	57.2	15.0	26–81	36.9	36.6	1–180	> 50	4

with a maximum emission peak at 365 nm, three times a week, starting with the dose of 1.0–1.25 J/cm² which was increased by 0.25 J/cm² every 3–5 treatments. Except for cases of total intolerance of psoralens, patient assignment to different therapeutic modalities: PUVA (following oral administration of 8-methoxypsoralen) or UVB 311 nm irradiation was random and resulted mainly from the availability of different modalities.

RESULTS

The characteristics of our patients did not differ significantly from other literature reports [2, 3, 5], possibly with the sole exception of men's representation which was slightly smaller in our study material than in other authors' (54 : 34). The age of the patients varied between 26 and 88 years. Similarly to other studies, the mean age was ~50 years in women and above 60 years in men (tables I and II). Results of treatment are presented in table III. Importantly, complete remission of skin lesions was obtained in all the patients regardless of the therapeutic modality, the duration of the disease and the extent of skin changes. To achieve the regression of lesions with UVB 311 nm irradiation, an average of 29.9 treatments were neces-

sary, which corresponds to an average of 22 J/cm² and 10 weeks of therapy. For PUVA, the respective figures were 23.7; 43.6 J/cm² and 7.9 weeks. None of the patients had to discontinue therapy due to adverse reactions. The relapse of the condition was seen after an average of 12.2 months in the UVB 311 nm group and after 13.8 months in the PUVA group.

DISCUSSION

PUVA has been known as an effective method of SPP treatment since the late 1970s. In 1976, Gilchrist *et al.* [7] published a report on the efficacy of photochemotherapy in the treatment of *mycosis fungoides*. Irrespective of the current views among dermatologists, small plaque parapsoriasis was classified for many years in the group of cutaneous T-cell lymphomas. Consequently, PUVA was recognized as the main therapy for parapsoriasis, small plaque parapsoriasis included.

In 1999, Hofer *et al.* [8] announced the results of UVB 311 nm treatment of 14 patients with SPP and 6 patients with MF. Complete remission of lesions was achieved in all the SPP patients after 14–27 irradiation sessions. Similarly effective outcomes for narrow-band UVB therapy were noted in 16 patients with SPP by Herzinger

Table III. Results of therapy with PUVA and UVB 311 nm in SPP

Methods	Number of irradiation treatments		UV dose [J/cm ²]		Number of weeks of therapy		Complete remission of skin lesions		Relapses [months]			
	Mean	Scatter	Mean	Scatter	Mean	Scatter	N	%	N	%	Mean	Scatter
UVB 311 nm	29.9	11–68	22	4.6–42.2	10	4–23	55	100	32	60.3	12.2	1–36
PUVA	23.7	12–60	43.6	15–78	7.9	4–20	35	100	21	60	13.8	1–72

et al. [9]. The reports quoted above are fully consistent with our observations. Complete remission of cutaneous lesions was obtained in all our patients, both in the PUVA and UVB-311 groups. In our study material, patients needed between 11 and 68 UVB 311 nm irradiation treatments (mean: 29.9, 22 J/cm²) to achieve remission. The finding is thus perfectly consistent with the observations made by Herzinger *et al.* [9], who used 19–50 treatments (mean: 32), and Aydogan *et al.* [10]. UVB 311 nm proved to be equally beneficial as PUVA in the treatment of 45 patients with LPP and 17 patients with SPP in the study by Duarte *et al.* [11]. In the report by Hofer *et al.* [8] the number of treatments ranged between 14 and 29 (mean: 20). The dose of UVB 311 nm radiation which was necessary to achieve remission in our study (22 J/cm²) was also similar to that applied by other authors [8–10]. There are also reports on isolated cases of fully effective SPP treatment using UVB 311 nm irradiation [4, 12, 13], however not all authors describe remissions in 100% of patients after a course of UVB 311 nm phototherapy. Aydogan *et al.* [10] achieved complete remission in 33 out of 45 treated patients (73.3%). Generally, however, both our observations and literature reports point to an outstanding, comparable to PUVA, efficacy of UVB 311 nm therapy in SPP patients. A total of 47 patients in the study group had previously been treated either with PUVA or UVB 311 nm, and the therapy administered during the study represented a consecutive course of treatment. In all these cases, however, the response to treatment was equally good. Considering the inconvenience of treatment to patients (length of therapy), UVB 311 nm irradiation does not differ significantly from PUVA. In our study material, PUVA treatment lasted an average of 7.9 weeks, while UVB 311 nm treatment – 10 weeks. However, taking into account adverse reactions of varying severity that are associated with PUVA (psoralen intolerance), UVB 311 nm therapy was definitely more patient-friendly. Similarly to reports by other authors [8, 10], treatment was followed by relapses: in 60.3% of patients treated with UVB 311 nm, after an average of 12.2 months (2–36), and in 60.0% of patients treated with PUVA, after an average of 13.8 months (1–72). The length of the remission period was thus similar for both therapeutic modalities.

Cutaneous lymphomas are also treated with narrow-band UVA-1 (340–400 nm) phototherapy, both at medium and high doses [14]. In 2000, a report presenting a case of SPP treatment based on UVA-1 irradiation was published [15]. Medium doses of UVA-1 (50 J/cm²/session) produced a complete remission of skin lesions after 15 treatments. There are no reports, though, on a more widespread use of this method. Considering the availability of PUVA and UVB 311 nm, the two modalities seem to be currently the most popular

methods of SPP treatment. Our study provides evidence for the equivalent efficacy of both irradiation therapies both in terms of immediate efficacy and influence on the length of the remission period. Since SPP is a disease known to persist for many years, with multiple recurrences necessitating consecutive courses of treatment, it seems justified to recognize UVB 311 nm irradiation as the therapy of choice in this indication.

An essential question remains with regard to the influence of both UV-based therapies on the potential of SPP transformation into MF. Japanese authors who analyzed large plaque parapsoriasis found no differences between PUVA and UVB 311 nm treatments in terms of the timing of active tumour development. As mentioned in the introductory section, the currently prevailing view is that SPP, as opposed to LPP, has no potential to transform into *mycosis fungoides*. Nevertheless, reports on isolated cases of such transformations must be considered [5, 6]. Likewise, it does not seem justifiable to fully ignore reports on the clonal proliferation of T cells observed in SPP, scanty as they are, which emerged in the mid-1990s [16–18]. There is, furthermore, a possibility of incorrect primary diagnosis. All these aspects considered, small plaque psoriasis seems to be a condition requiring treatment. Out of all currently available therapeutic regimens, the safest option ensuring efficacy similar to PUVA is UVB 311 nm irradiation.

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