

EXPERIENCE OF PHOTOTHERAPY IN DERMATOLOGICAL PRAXIS IN COMPLEX THERAPY OF PSORIASIS PATIENTS

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Psoriasis is a chronic relapsing skin disease presenting with erythematous and papulous lesions with infiltration and extensive desquamation on the skin surface. It is a genetically determined, multifactorial dermatosis where genetic, immune, and environmental factors play significant roles in its development. In Latvia in treatment of different forms of extensively spreading psoriasis, PUVA (psoralen and ultraviolet A light therapy), a combined method, is administered, applying long-wave UVA radiation with wavelength 320–400 nm in combination with photosensibilisator 8-metoxypsoralen and medium wave length UVB radiation narrow-band phototherapy — 311 nm using specialised TL-01 lamps. The aim of our clinical investigation was to determine the efficacy of narrow-band phototherapy (UVB 311 nm) in the complex treatment of patients with different severity of extensive psoriatic lesions treated in the Clinical Centre of Skin and Sexually Transmitted Diseases. Cases of clinical data of 260 patients with widely spread psoriasis were analysed. In the Group 1 (n = 102) receiving narrow-band UVB therapy, the mean and cumulative UVB dosage was 1.8 ± 0.6 and 21.5 ± 3.8 J/cm², respectively, whereas in Group 2 (n = 91) it was 2.2 ± 0.1 and 27.7 ± 8.0 J/cm². To obtain clinical recovery, 18 to 30 procedures were necessary (average 22 ± 4.1) with total irradiation dose received 110 ± 4.6 J/cm². In 67 patients of the control group, PUVA therapy was administered, and positive therapeutic efficacy was observed in all patients. Clinical recovery was obtained in 86.2% in patients of the Group 1, in 82.4% — of Group 2, and in 80% — in 67 patients of the control group. Narrow-band (311 nm) UVB phototherapy is currently one of the leading pathogenetical methods of treatment of patients with widespread psoriasis. It has high efficacy, good tolerability, does not have severe side effects and restrictions in use, in comparison with traditional PUVA therapy.

Key words: psoriasis, UV therapy, phototherapy, PUVA (combination of psoralen and long-wave ultraviolet radiation), PASI (Psoriasis Area and Severity Index).

INTRODUCTION

Psoriasis is a chronic relapsing skin disease, affecting 0.2–4.8% of the world population. The lowest prevalence is in Asian countries, and the highest — in Scandinavia (Duffin *et al.*, 2010), in the Baltic countries — 4% (Ivdra, 2010). It is a genetically determined, multifactorial dermatosis and significant role in its development is played by genetic, immune, and environmental factors (Hartmane, 2004). Clinical presentations of the disease are erythematous and papulous lesions with infiltration and extensive desquamation on the surface. Nowadays, it has been proved

that keratinization, the main function of the epidermal layer of the skin, has the crucial significance in the pathogenesis of psoriasis that is determined by apoptosis of keratinocytes, as well as alteration in the process of proliferation and differentiation of these cells. Such changes explain the numerous immunological conceptions of the development of psoriasis (Bowcock and Krueger, 2005). The leading immunopathogenetical mechanism is psoriasis migration of T lymphocytes with lymphocytary antigen in the skin after their common interaction with epidermal antigen presenting cells in regional lymph nodes. The skin infiltrating T-lymphocytes, monocytes, macrophages, and keratinocytes

produce anti-inflammatory cytokines that promote hyperproliferation of keratinocytes and alterations in their differentiation (Hartmane *et al.*, 2001). Therefore, the main pathophysiological processes in psoriasis include hyperplasia of epidermis with alterations in differentiation of keratinocytes as well as inflammatory reaction in dermis.

One of the most effective methods of psoriasis treatment is different spectrum (according to wavelength) ultraviolet (UV) radiation therapy or phototherapy (Lapolla *et al.*, 2011). In Latvia in treatment of different forms of extensively spreading psoriasis, PUVA (a combined method, psoralen and UVA treatment), is administered, applying long-wave UVA radiation with wavelength 320–400 nm in combination with photosensibiliser 8-metoxypsoralen and medium wave length UVB radiation narrow-band phototherapy — 311 nm using specialised TL-01 lamps (Anonymous, 2014). The substantiation of the efficacy of phototherapy is its immunomodulatory influence with the prevalence of immunosuppression (Ulrich and Byrne, 2012). The main immunologic effects of phototherapy are:

- 1) induce apoptosis or programmed cell death in cells pathogenically responsible for development of psoriasis (Langerhans cells in epidermis, dendritic cells in the skin, keratinocytes, T lymphocytes);
- 2) suppress the activity of adhesion molecules on antigen presenting cells;
- 3) inhibition of mitotic activity of T lymphoid cells in the skin and dermal capillaries;
- 4) promote production of immunosuppressive and anti-inflammatory mediators and cytokines.

Several publications have demonstrated that narrow-band UV radiation therapy has more intensive immunosuppressive and anti-inflammatory action (Kostovic and Pasic, 2004; Parsed *et al.*, 2006). Absolute contraindications in phototherapy are genetic pathologies with increased light sensitivity with consecutive higher risk for development of skin cancer, hard-going somatic diseases in decompensated stages. Prior to start of UV therapy, it is recommended to determine the individual light sensitivity, specifying the minimal erythemal dose (MED) (Barbagallo, 2001). In dermatological praxis in predominant cases, standardised therapeutic schemes are applied, starting with a single dose of phototherapy and then increasing the dose, taking into account the phototype of the skin (Menter *et al.*, 2010, Archier *et al.*, 2012). In Latvia phototherapy is administered, based on standardised guideline protocols based on phototype of the skin, not determining the individual MED (Anonymous, 2013).

The aim of our clinical investigation was to determine the efficacy of narrow-band phototherapy (UVB 311 nm) in the complex treatment of patients with different severity of extensive psoriatic lesions treated in Clinical Centre of Skin and Sexually Transmitted Diseases from 2008 till 2013.

MATERIALS AND METHODS

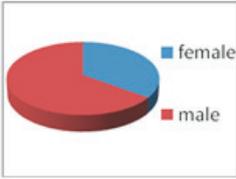
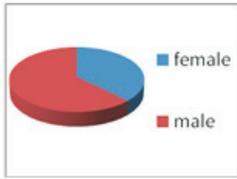
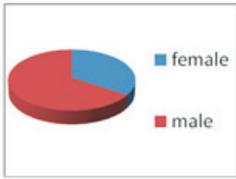
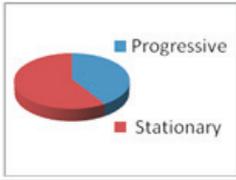
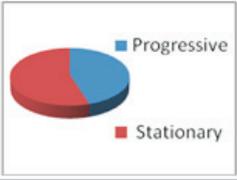
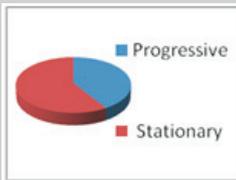
Patients. Cases of clinical data of 260 patients with widely spread psoriasis were analysed. Of these, 167 were male and 93 were female patients, with age 14 to 72 (mean age 28 ± 11.4 years). Duration of the disease varied from 7 months to 36 years (mean duration 16.0 ± 7.8 years). *Psoriasis vulgaris* form was diagnosed in 187 (72%) patients, but *psoriasis exudativa* form in 73 (28%) patients. Disease in the progressive stage was detected in 62 (24%) and in stationary stage in 156 (60%) patients. Torpid stage was diagnosed in 42 (16%) patients, presenting with exacerbations from 2 till 5 times per year having short periods of remission from 3 weeks till 4.5 months, as well as slow remission of psoriatic lesions during the treatment period. Narrow-band UVB phototherapy was used to treat 193 patients (106 male and 87 female), aged from 14 to 68 years and the duration of the disease from 7 months to 34 years. For analysis of clinical data, patients were divided into two groups and a control group, taking into account the grade of severity of psoriasis (Fig. 1). Group 1 (major group) included 102 patients with mild and medium forms of psoriasis, whose PASI (Psoriasis Area and Severity Index) at the start of treatment were from 7 till 18 points. Group 2 (comparison group) included 91 patients with severe psoriasis with PASI varying from 22.0 to 48.6 points. There were 67 patients in the control group.

Procedures. Narrow-band (311 nm) UVB phototherapy procedures were performed 2 to 5 times a week, in line with the accepted protocol. The starting UV radiation dose was $0.1\text{--}0.2\text{ J/cm}^2$, depending on skin phototype. Radiation dosage was increased by 0.1 J/cm^2 in every next procedure. In case of development of mild erythema, the dosage remained the previous.

Phototherapy was performed in complex with systemic anti-inflammatory and local medications for treatment of psoriasis — via intravenous infusions of *Sol. Haemodesi* and *Sol. Natrii chloridi* 0.9%, 10% *Sol. Calcii gluconatis*, 30% *Sol. Natrii tiosulphatis*. Topical antipsoriatic creams and ointments were applied.

In the control group, data of 67 psoriasis patients (44 male and 23 female) treated with PUVA therapy were analysed. Age of patients in this group varied from 18 to 72 years; duration of the disease was from 3 to 36 years. For these patients the PASI index before the start of therapy varied from 24.0 to 50.9 points. PUVA therapy procedure was performed 2–3 times a week according to the treatment protocol. In these cases, a photosensitising agent — 8-metoxypsoralen (meladinin) was administered 1 hour before UV irradiation *0 per os* in dosage 0.6 mg/kg. The initial dosage of irradiation was $0.3\text{--}0.75\text{ J/cm}^2$. In the consecutive UVA irradiation procedures dosage was increased after every 1–3 procedures by $0.25\text{--}0.5\text{ J/cm}^2$.

Both groups of patients treated with narrow-band UVB phototherapy statistically did not differ from the control group that received PUVA therapy. These groups did not differ in

Parameters	UVB (311nm) (PASI < 20) Group 1 (n=102)	UVB (311nm) (PASI > 20) Group 2 (n=91)	PUVA Comparison group (n=67)
Age	26.5±12.0 (14- 62) years	29.7±11.4 (16-68) years	30.7±12.9 (18- 72) years
Male/ female	66/37 	57/34 	44/23 
Duration of disease (years)*	12± 7.7 7 months-28 years	8.3±12.6 (3 – 26 years)	11.9±9.5 (5- 36 years)
Form of psoriasis:	Vulgaris 77 (75.4%) Exsudativa 25 (24.5%) 	Vulgaris 62 (68.1%) Exsudativa 29 (31.8%) 	Vulgaris 47 (70.1%) Exsudativa 20 (29.8%) 
Stage of the disease:	Progressive 42 (41.1%) Stationary 60 (58.8%) 	Progressive 41 (45%) Stationary 50 (54.9%) 	Progressive (28 (41.8 %) Stationary 39 (58.2%) 
PASI index	10.2±9.4	24.6±8.8	28.6±11.3

Remark. *- mean error ($M \pm m$)

Fig. 1. Clinical parameters of psoriasis patients

age, or in the form of psoriasis, or in the duration of the disease. Patients from Group 2 and the control group were comparable by means of severity of onset of the disease. Clinical manifestation of psoriasis was evaluated in the beginning and at the end of the treatment course. The efficacy of treatment was detected taking into account the stage of regression of psoriatic lesions (Table 1).

Data processing methods. Statistical analysis of clinical data and obtained results was performed, determining the arithmetic mean (M), average arithmetic error (m) and average square deviation (s). To define statistically significant differences among the mean values, Student (t) coefficient and non-parametric batch file criterion were applied. To evaluate the efficacy of therapy the changes in PASI values were compared between the two groups of patients, treated with UVB phototherapy and PUVA. T test was applied to compare two independent selections. Significant differences were considered if $p < 0.05$. Before application of the comparison test the correspondence of all the selections to nor-

Table 1

CRITERIA OF EFFICACY OF PHOTOTHERAPY

Criterion	Clinical description
Clinical recovery	Total regress of psoriatic lesions
Obvious improvement	Regress < 85% of lesions; in the biggest psoriatic plaques persistent infiltration
Improvement	Regress > 85% of lesions; in the biggest psoriatic plaques insignificant infiltration
Without efficacy	Resolution of psoriatic lesions 15%

mal distribution was checked by non-parametrical one factor test of Kolmogorova–Smirnova, as well as by percentile and quartile — P-P and Q-Q curves.

Duration of treatment course with narrow-band middle wave length UVB therapy (311 nm) was individual and depended on the speed of absorption of psoriatic lesions and time of regression onset. In Group 1 receiving narrow-band

Table 2

DOSAGES OF NARROW-BAND UVB AND PHOTOTHERAPY

Indication	UVB (311 nm) (PASI < 20)	UVB (311 nm) (PASI > 20)	PUVA
Initial irradiation dose (J/cm ²)	0.1- 0.2	0.1- 0.2	0.3- 0.75
Maximal irradiation dose (J/cm ²)	1.8±0.6	2.2±0.1	6.9±1.9
Total irradiation dose (J/cm ²)	21±3.8	27.7±0.8	110±4.6
Number of procedures in treatment course*	20±4.5	25±5.2	22±4.1

UVB therapy the mean and cumulative UVB dosage was respectively 1.8 ± 0.6 and 21.5 ± 3.8 J/cm², whereas in Group 2 — 2.2 ± 0.1 and 27.7 ± 8.0 J/cm². The number of procedures in Group 1 varied from 10 to 25 (average 20 ± 4.5), in Group 2 from 20 to 35 (average 25 ± 5.2) (Table 2).

RESULTS

Regress of the psoriatic process was observed on average after 10–12 procedures. In 142 (74%) of patients, resolving of psoriatic lesions started from the peripheral part of lesions, and in 51 (26%) from the centre of the lesion. Smaller elements with minor infiltration resolved and regressed faster than those lesions with deeper infiltration. Obvious positive improvement was detected in lesions localised on the face, trunk and upper extremities. Slower resolving and regress of psoriatic lesions were observed in lesions localised on lower extremities. Positive efficacy of therapy was observed in all patients who received UVB phototherapy (Fig. 2). The overall tolerance of phototherapy was good. In

14 (7.2%) patients, barely susceptible erythema was observed, and in 8 (4.1%) — moderate severe itching of skin.

After administering PUVA therapy, positive therapeutic efficacy was observed in all patients (Fig. 2). To obtain clinical recovery, 18 to 30 procedures were necessary (average 22 ± 4.1) with total irradiation dose received 110 ± 4.6 J/cm². No statistically significant differences were observed in a number of therapeutic procedures between the patients who received UVB therapy and the patients who received PUVA therapy (control group) ($p > 0.05$) (T test for comparison of two independent groups). However, in the case of PUVA therapy, the number of side effects was more numerous and more severe. Twelve (17.9%) patients developed erythema and moderate itching of the skin, five (7.4%) patients had headaches and eight (11.9%) of patients suffered from nausea as a side effect of photosensibilising medication.

Clinical recovery was obtained in 86.2% of patients of Group 1, in 82.4% of Group 2, and in 80% of patients of the control group.

Statistically significant differences in PASI percentage improvement were not observed between groups of patients who received narrow-band UVB 311 nm and phototherapy ($p > 0.05$) (Fig. 2) (T test to compare two independent groups).

DISCUSSION

The obtained results show the high clinical efficacy of the narrow-band middle wavelength (311 nm) UVB phototherapy in the treatment of patients with widespread psoriasis. By efficacy, this method is not weaker than the slightly

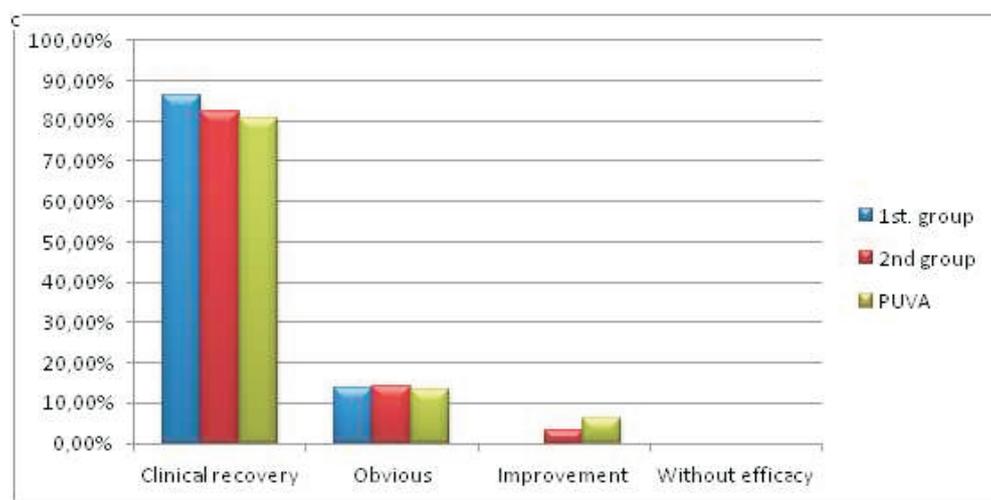


Fig. 2. Clinical results of UVB (311 nm) and PUVA therapy in patients with widespread psoriasis

older method of traditional PUVA therapy. Furthermore, there were less patients in the control group (see the comparative literature data on UVB and PUVA therapy, Archier *et al.*, 2012). By applying PUVA photochemical treatment, remission of psoriasis was achieved by controlled induction of photochemical reactions in the skin, which was achieved by UVA-induced photo activation of psoralens. The major problem of PUVA therapy is the risk of development of numerous long-term side effects caused by photochemical reactions. The most common of them are premature aging of the skin and photocarcinogenesis. Signs of premature aging caused by PUVA therapy are dryness and wrinkling of the skin, and development of telangiectasias and keratosis, which are irreversible and aesthetically unacceptable for patients. Moreover, non-melanoma skin cancer in patients after administration of PUVA phototherapy develops 10 times more often than in the overall population. Several publications have confirmed increased risk for the development of melanoma as the result of received PUVA therapy. Studies on animals have shown carcinogenic effect of UVB and the premature aging of the skin, although when compared to PUVA, the risk of development of skin cancer was obviously lower. Narrow-band UVB phototherapy has been more often administered in the dermatological praxis at the Clinical Centre of Skin and Sexually Transmitted Diseases during the last three years. Unlike PUVA therapy, in the case of UVB therapy it is not necessary to administer photosensitising medication, thus decreasing the number of side effects.

Our study showed that to achieve remission of psoriasis, an equal number of UVB and PUVA procedures were necessary. Furthermore, the dose of UVB was significantly lower than the dose of UV radiation received during PUVA therapy (Table 2). Due to the smaller dose of UVB radiation, the number of cases of development of erythema as a therapy side effect was lower. Thus, UVB phototherapy was better accepted by patients. The advantage of UVB therapy is that this method can be prescribed to psoriasis patients to whom PUVA therapy is contraindicated due to other somatic diseases. Narrow-band UVB phototherapy in comparison to PUVA is economically more cost-effective, it does not require psoralens, it can be prescribed to pregnant patients and children under 18 years of age, and there is no necessity for eye protection during treatment period (Dawe, 2003).

After analysis of data from the Clinical Centre of Skin and Sexually Transmitted Diseases it can be concluded that narrow-band (311 nm) UVB phototherapy currently is one of the leading pathogenetical methods of treatment of patients with widespread psoriasis. We recommend UVB phototherapy as the method of choice in the treatment of moderate and severe forms of psoriasis, as it is as effective as PUVA, it is better tolerated and has fewer side effects.

PUVA is recommended in cases of an infiltrative form of psoriasis, as UVA radiation penetrates deeper into human

skin than UVB. PUVA therapy if preferable in cases when a patient presents long-term torpid occurrence of psoriatic lesions, shows photosensibilisation against UVB, and has active aggressive onset of psoriasis with inflammatory component.

CONCLUSIONS

Narrow-band UVB phototherapy has high efficacy, good tolerability, and does not have severe side effects and restrictions in use, in comparison with traditional PUVA therapy. It has to be the method of the first choice for treatment of moderate and severe psoriasis.

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FOTOTERAPIJAS LIETOŠANAS PIEREDZE DERMATOLOĢISKAJĀ PRAKSĒ PSORIĀZES PACIENTU KOMPLEKSĀ ĀRSTĒŠANĀ

Psoriāze ir hroniski un recidivējoši norisoša, ģenētiski nosacīta, multifaktoriālas dabas ādas slimība, un tās attīstībā liela nozīme ir ģenētiskiem, imūniem un ārējās vides faktoriem. Klīniski psoriāzes gadījumā ir izplatīti eritematozi un papulozi infiltratīvi bojājuma perēkļi ar izteiktu lobīšanos. Latvijā psoriāzes izplatītu formu ārstēšanai ordinē PUVA (psoralēns un ultravioletais starojums A), tā ir kombinēta metode, lietojot garo viļņu UVA starojumu 320–400 nm un fotosensibilizatoru 8-metoksipsoralēnu un vidēja garuma viļņu UVB starojuma šaura spektra fototerapiju – 311 nm ar specializētām TL-01 lampām. Tomēr šaurā spektra UV starojuma terapijai (UVB 311 nm) piemīt izteiktāka imūnsupresīva un pretiekaisuma iedarbība. Mūsu klīniskā darba mērķis bija noskaidrot šaurā spektra fototerapijas (UVB 311 nm) efektivitāti kompleksas ārstēšanas gaitā pacientiem ar dažāda smaguma izplatītiem psoriātiskiem bojājumiem, kuri ārstējās Ādas un seksuāli transmisīvo slimību klīniskajā centrā. Tika apkopoti un analizēti 260 pacientu ar izplatītu psoriāzi klīniskie dati. Analizējot klīniskos datus, pacienti tika sadalīti divās grupās, ņemot vērā psoriāzes smaguma pakāpi. Pirmajā grupā tika iekļauti 102 pacienti ar vieglu un vidēji smagu psoriāzi, kuriem PASI (psoriāzes bojājuma izteiktības indekss) terapijas sākumā svārstījās no 7 līdz 18 punktiem. Otrā grupā ietilpa 91 pacients ar smagi norisošu psoriāzi. Šiem pacientiem PASI variēja no 22,0 līdz 48,6 punktiem. Šaurā spektra vidējā viļņu garuma UVB terapijas (311 nm) kursa ilgums bija individuāls un atkarīgs no psoriātiskā bojājuma uzsūkšanās un regresa iestāšanās laika. Pirmajā šaurā spektra pacientu terapijas grupā vidējā un kumulatīvā UVB starojuma deva tika noteikta attiecīgi 1.8 ± 0.6 un $21.5 \pm 3.8 \text{ J/cm}^2$, otrajā grupā attiecīgi 2.2 ± 0.1 un $27.7 \pm 8.0 \text{ J/cm}^2$. Kontrolgrupai tika izmantoti 67 (44 vīrieši un 23 sievietes) psoriāzes pacientu dati, kuri tika ārstēti, lietojot PUVA terapiju. Pozitīva terapijas efektivitāte tika konstatēta visiem pacientiem, kuri saņēma UVB fototerapiju. Klīniskā izvēlešanās tika sasniegta 86.2% pirmās grupas pacientiem, 82.4% otrās grupas pacientiem un 80% kontrolgrupas pacientiem. Šaurā spektra (311 nm) UVB fototerapija mūsdienās ir viena no vadošajām patoģenētiskās ārstēšanas metodēm pacientiem ar izplatītu psoriāzi. Tās efektivitāte ir augsta, panesamība laba, kā arī tai nepiemīt blaknes un lietošanas ierobežojumi, salīdzinot ar tradicionālo PUVA terapiju.