Symposium - Psoriasis

Narrowband ultraviolet B in the treatment of psoriasis: The journey so far!

Sunil Dogra, Dipankar De

Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence: Dr. Sunil Dogra, Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, India. E-mail: sundogra@hotmail.com

DOI: 10.4103/0378-6323.72461

ABSTRACT

Ever since artificial TL-01 lamps were developed, narrowband ultraviolet B (NBUVB) has gained giant strides in dermatology. Psoriasis is one of the common indications for the use of NBUVB in present day dermatology. We discuss here the evolution of NBUVB, its mechanism of action pertaining to psoriasis, indications and contraindications, dosimetry, complications of NBUVB while being used in patients with psoriasis, its merits and demerits in comparison with broadband UVB and psoralen+UVA (PUVA), and recent developments in the delivery system of NBUVB.

Key words: Narrowband ultraviolet B (NBUVB), broadband UVB, psoriasis

INTRODUCTION

Ultraviolet (UV) light comprises a narrow band in the electromagnetic spectrum consisting of wavelengths between around 100 nm to up to 400 nm (UVC: 200–280 nm; UVB: 280–320 nm; UVA: 320–400 nm). UV light of shorter wavelengths is absorbed in the earth's atmosphere and only UV of longer wavelengths (UVA, UVB and minimal amount of UVC) reach the earth's surface. UV light in the sunlight has been known to cure dermatological as well systemic diseases for ages. However, narrowband UVB (NBUVB) is a relatively recent but efficient introduction into dermatologic practice.

EVOLUTION OF NBUVB

UVB in combination with coal tar preparations is one of the oldest treatments for psoriasis. The Goekerman regimen introduced in 1925 comprises of UVB in addition to crude tar, an antimitotic agent and a photosensitizer.[1] Broadband UVB (BBUVB) was used for quite sometime in the management of psoriasis after it had been introduced in 1978 by Wiskeman.[2] However, it never gained popularity due to its erythemogenic potential and lesser efficacy. The breakthrough in the use of UVB came in 1977 when Fischer, while examining the efficacy of wavelengths from 254 to 405 nm for the treatment of psoriasis, noted that a narrow band of UVB at 313 nm wavelength is notably effective for clearance of disease, particularly at higher doses, without producing significant erythema.[3] Parrish and Jaenicke discovered that clearance of psoriasis lesions occurred at wavelengths between 296 and 313 nm, with a better response at a wavelength of 313 nm.[4] These findings gave impetus for the development of artificial fluorescent lamp containing phosphor (TL-01) producing peak emission at a narrow band of 311 nm (±2 nm). This development ushered in the era of new phototherapeutic modality (NBUVB) and several studies on its use in psoriasis and various other dermatoses followed. The first clinical use of this commercially available fluorescent lamp dates back to 1988 when van Weelden *et al*.[5] and Green *et al*.[6] used it in the treatment of psoriasis. Subsequently, it has been used in indications other than the one it was developed for; vitiligo, atopic eczema and mycosis fungoides being the more common ones.

MECHANISM OF ACTION OF NBUVB IN PSORIASIS

The exact mechanism of action of NBUVB is not

How to cite this article: Dogra S, De D. Narrowband ultraviolet B in the treatment of psoriasis: The journey so far!. Indian J Dermatol Venereol Leprol 2010;76:652-61.

Received: Decemer, 2009. **Accepted:** June, 2010. **Source of Support:** Nil. **Conflict of Interest:** None declared.

known. Several genetic and molecular factors are induced by NBUVB. The most significant molecular target of NBUVB is cellular DNA. Absorption of UVB by nucleotides of nuclear DNA leads to DNA photoproduct formation, mainly pyrimidine dimers. These photoproducts interfere with cell cycle progression and induce growth arrest. This mechanism is considered to be most important in treatment of psoriasis, with reduction in the dividing cells of basal layers as well as suprabasal epidermis. UVB also induces prostaglandin release and alters cytokine expression and secretion.[7] NBUVB decreases expression of type 1 cytokine interferon-α and its inducers interleukin (IL)-12, IL-18 and IL-23 in the lesional skin.[8] UVB rays reduce natural killer cell activity and also deplete the immunocompetent T-cells from the epidermis and dermis by inducing apoptosis.[9] NBUVB suppresses the functions of antigen presenting cells in addition thus inhibiting the ability of these cells to present antigens. The newly discovered T cell subset, the Th17 cells, considered to be in the center stage of psoriasis pathogenesis are also down-regulated.[10] Therefore, in addition to suppressive effect on keratinocytes, NBUVB also results in immunomodulation. On a per-photon basis, UVB possesses more energy but, due to its shorter wavelength, it has superficial penetration and affects only epidermal keratinocytes and Langerhans cells.

INDICATIONS OF NBUVB IN PSORIASIS

Conventionally, NBUVB is indicated in generalized psoriasis involving more than 10% of the body surface area. It can be used even in psoriasis involving limited areas of the body but not responding to topical treatment and involvement of areas that are causing physical or psychological morbidities, like hands and feet.[5-7]

CONTRAINDICATIONS OF NBUVB IN PSORIASIS

Generally, NBUVB is contraindicated in patients who have any photosensitive condition, and in those with a predisposition or actually having a history of cutaneous malignancies. These conditions include lupus erythematosus, xeroderma pigmentosum, those who have received arsenic in any form or ionizing radiation therapy and history of previous melanoma or multiple non-melanoma skin cancers. The other relative contraindications may be practical difficulties like claustrophobia or inability to stand in the phototherapy chamber through the session due to age or disability.[5-7]

DOSIMETRY AND FREQUENCY OF EXPOSURE OF NBUVB IN PSORIASIS

The optimum phototherapy regimen is to achieve a complete clearance of psoriasis with a minimum number of exposures, a low cumulative UV dose and with least possible acute as well as chronic side-effects. What should be the initial dose of exposure, how frequently should a patient be exposed to phototherapy, what should be the percentage increase in the UV dose in every subsequent visit, what should be the maximum dose a patient should be subjected to and what if somebody develops adverse effects of NBUVB? Although answers to these riddles are still evolving over the years, these aspects of NBUVB phototherapy have largely been addressed.[5-7]

Basic instructions and education about phototherapy should be given to all patients. These include use of eye protecting goggles, shielding genitalia in male patients and avoiding unnecessary exposure to sunlight. Protection of chronically exposed skin like face and dorsa of hands, if not involved, by using proper clothing and appropriate sunscreens should be advised.[5-7]

The most important extraneous variables that can influence the outcome of any phototherapy treatment are the spectral content of the UV source employed and UV energy incident on the patients' skin. Fluorescent UV tubes are known to wear out with time, and this fact can influence the therapeutic outcome. Taylor *et al.*,[11] on behalf of the British Photodermatology group, have put forward some recommendations regarding calibration for optimum results of UV phototherapy. All phototherapy units should have UV radiometers to measure irradiances and the meter should be calibrated annually. Some phototherapy chambers have in-built UV radiometers and reading with this meter should match closely with the directly measured irradiance values. Measurement of irradiance every 25–50 h of use is acceptable. However, after installation of new lamps, it should be measured every 10–15 h of use, as lamps when new degrade more quickly.

In general, initial dose is calculated on the basis of minimal erythema dose (MED) determined prior to start

of phototherapy. MED is determined 24 h after exposure of around 1 cm × 1 cm areas on the upper back/buttocks to a pre-set test dose ladder with geometric escalation of UV dose according to skin phototype. MED is taken as the lowest UVB dose producing defined perceptible erythema at the test site.

Initial dose of treatment is generally 70% of the MED. Hofer *et al*.[12] in their study comparing phototherapy with near (70% of MED) vs. far (35% of MED) erythemogenic dose of NBUVB as initial treatment dose in psoriasis observed that near-erythemogenic treatment cleared psoriasis faster. However, to achieve a satisfactory response with the far-erythemogenic regimen, only four excess treatments compared with the near-erythemogenic dose regimen were necessary on an average, and the cumulative dose was significantly lower. The observation of Kleinpenning *et al*.,[13] however, was different. When they compared response in psoriasis patients treated with an initial dose of 70% of MED followed by 40% dose increments vs. those treated with 35% MED and followed by 20% dose increments, no significant difference was found in the number of patients achieving clearance in either of the groups. The high-dose group required four fewer treatment sessions without any significant difference in cumulative dose required to achieve clearance. In India, pre-irradiation MED is not determined at most of the centers and a starting dose employed in few published studies seems to have underestimated the initial starting dose. There are very limited and contradictory data on MED determined on type 4/5 Indian skin. Pai *et al*.[14] determined the average MED in type 4 skin to be 600 mJ/cm^2 and in type 5 skin to be 1100 mJ/cm^2. In a small series of six south Indian volunteers, Serish and Srinivas[15] observed MED to vary widely between 150 mJ/cm^2 and 400 mJ/cm^2. In another study, the average MED in Indian skin (type 4/5) was determined to be around 1,000 mJ/cm^2.[16] According to recent guidelines by the American Academy of Dermatology (AAD) for treatment of psoriasis, the initial dose can be adjudged by skin type (not a MED-based one). In the skin type-based regimen, the initial NBUVB doses recommended are 130, 220, 260, 330, 350 and 400 mJ/cm^2 for skin types 1 through 6, respectively. If MED is determined, the initial dose should be 50% of MED.[17]

In general, the dose increment in NBUVB depends on erythema response. The erythema response is assessed before the next phototherapy session and can be graded as no erythema, mild and barely perceptible erythema (grade 1), moderate and well-defined asymptomatic erythema (grade 2) and severe painful erythema persisting for more than 24 h (grade 3). In case there is no erythema, the dose is increased by 20% of the last dose. In the presence of grade 1 erythema, the previous dose is maintained and subsequent dose increment is reduced to 10%. In case of grade 2 erythema, postpone one treatment, repeat previous dose at next visit and reduce to 10% increment, while in case of grade 3 erythema, no treatment is offered until recovery and further treatment is given by reducing exposure dose by half and 10% increment thereafter.[18] Wainwright *et al*.[19] have demonstrated that the total dose required for disease clearance was lower in the low-increment (10%) side than the high-increment (20%) one. The median number of treatments required was marginally higher (21 vs. 20.5) in the low-increment side. The time taken for psoriasis to relapse was similar in both the regimens. Boztepe *et al*.[20] have reported no difference in response rates as well as number of sessions with either 20% or 5–10% increments. But, both the median maximum dose and the cumulative dose to achieve response were significantly higher with 20% escalations. The AAD recommends pre-determined dose increment according to skin prototype; 15, 25, 40, 45, 60 and 65 mJ/cm^2 for skin types 1 through 6, with a maximum dose of 2,000 mJ/cm^2 for skin types 1 and 2; 3,000 mJ/cm^2 for types 3 and 4 and 5,000 mJ/cm^2 for types 5 and 6. If pre-treatment MED is determined, the dose increment should be 10% of the initial MED for the initial 20 exposures and as per physicians' discretion thereafter.[17]

The frequency of exposure to NBUVB is generally thrice to five-times a week.[21] The efficacy of twice-weekly vs. four-times a week as well as three vs. five-times a week have been assessed in psoriasis. Dawe *et al*.[22] observed that phototherapy with erythemogenic doses applied 3/week vs. 5/week did not significantly change the clearance rate and duration of remission. The number of treatments and cumulative dose of UVB at clearance were significantly higher with the 5/week regimen. Similarly, Leenutaphong *et al*.[23] in their comparative study of low-dose NBUVB (50% MED starting dose) with exposures 2/week vs. 4/week observed that clearance rate and duration required for clearance of psoriasis were comparable in both the groups. Twice-a-week treatment is convenient for the patient and two to three groups of patients can be treated in a week instead of one group (4/week) in a single NBUVB chamber.

If dose is missed due to some reason or the other, the NBUVB can be restarted according to the following schedule: less than a week, maintain the last exposure dose; 1–2 weeks, restart at a dose <25% of the last dose; 2–3 weeks, restart at 50% depleted dose; for therapy interruption for more than 3 weeks, phototherapy should be restarted from the previous starting dose.[17]

NBUVB has gradually replaced BBUVB and is found to be equally efficacious to psoralen UVA (PUVA) in the management of psoriasis. In a relapsing disease like psoriasis, duration of remission after phototherapy is important as none of the phototherapy modality or systemic therapy is devoid of side-effects. Green *et al*.[6] reported that 38% of their NBUVB-treated patients were in remission after 1 year while Collins *et al*.[24] reported the corresponding figure to be 42% in their PUVA-treated patients. Post-treatment maintenance regimen (twice-weekly for the first 4 weeks and once-weekly for the next 4 weeks, totaling 12 exposures) helped 55% of the patients treated with NBUVB to remain in remission against 33% who did not receive it.[25]

COMPLICATIONS OF NBUVB

Erythema is the only significant short-term side-effect. Incidence of erythema with NBUVB, as can be speculated from its wavelength, seems higher than that with PUVA. However, incidence of therapy postponement as a result of erythema is higher with PUVA due to the persistent nature of erythema caused by it. The incidence of erythema is reported to vary from 10% to 94% according to treatment protocol.[26] Blistering has been reported to appear at the sites of psoriasis lesions during the treatment. It has been speculated that rapid decrease in acanthosis and desquamation overpowers the protective mechanisms, namely the induction of pigmentation and increase in the thickness of stratum corneum.[27] Appearance of plaque tenderness may be a valuable guide to impending blistering and the dose can be reduced to allow the non-acclimatized skin to adjust to the ongoing insult.[28] Pruritus has been mentioned as an occasional side-effect of NBUVB, although it may represent the pruritic nature of the underlying disease rather than being precipitated by phototherapy. Reactivation of orolabial herpes simplex may be problematic and precautionary measures would be prudent in those who are prone to frequent relapses. Exposure keratitis and conjunctivitis can occur following NBUVB exposure.[26] Although cataract formation is not a problem with NBUVB as is possible with PUVA, the eye protection protocol during UV exposure should be stringently followed. Tanning induced by NBUVB was recently assessed by Jo *et al*.[29] NBUVB-induced tanning was found to increase gradually during treatment, and post-treatment recovery required at least 10 weeks.

Little published data exists on the carcinogenic potential of NBUVB. Experiments in the mouse model suggest that cancer risk with NBUVB is probably less than that with PUVA.[30] In the same setting, it has been estimated that NBUVB is probably two to three-times more carcinogenic than BBUVB in equivalent doses. However, it is proposed that this disadvantage of NBUVB can be offset by the fact that the number of MEDs required for clearance of psoriasis is lower than that for BBUVB. Man *et al*.[31] in their study involving data of 1,908 patients treated with NBUVB over 15 years observed no increased risk of squamous cell carcinoma or malignant melanoma. The incidence of basal cell carcinoma (BCC) was marginally higher than expected. As some of the patients were diagnosed to have BCC within 3 months of starting NBUVB, it was concluded that NBUVB may not have been causally related to the development of BCC overall. In the retrospective study involving 195 psoriasis patients receiving either BBUVB or NBUVB, Weischer *et al*.[32] derived that neither of the modalities predispose to increased skin cancer risk. In a review of carcinogenic risk of phototherapy involving studies published in MEDLINE between 1966 and 2002, Lee *et al*.[33] concluded that they could not identify any human data on the risk of non-melanoma skin cancer with NBUVB to determine the clinical relevance.

NBUVB VS. BBUVB IN PSORIASIS

Fluorescent lamps (i.e., FS-20, TL-12) emitting light in the BBUVB range had broad spectral emission with some proportion (about 5.5%) of wavelength within the UVC range (<290 nm). In addition to these conventional BBUVB lamps, fluorescent lamps with little emission in the UVC range (0.5%) are also available, the so-called selective broadband UVB (UV6). NBUVB lamps emit 0.1% radiations below 290 nm.

Majority of the studies comparing the efficacy of BBUVB and NBUVB in psoriasis have demonstrated that NBUVB is better than BBUVB. The conclusion of

a recent metaanalysis of controlled studies was also similar.[22] It was observed that the maximal clearance response was produced after fewer treatments in the NBUVB group, and this difference could be appreciated only after 2 weeks of treatment.[34] On the contrary, there are also studies determining equal response to both treatment modalities. However, the time to satisfactory response and total duration of therapy were shorter in the NBUVB arm.[6] The main limitations with NBUVB are longer exposure times per session and four to six-times higher doses required to generate an equi-erythemogenic effect.[35]

There are only few studies comparing selective ultraviolet B (SUV, little emission below 290 nm) with NBUVB. In one side-to- side comparison study of NBUVB or SUV in combination with the Ingram regimen, the results were comparable in 60% of the patients, and in the rest, NBUVB was found to be more effective.[36] In another side-to-side comparison study, the modalities were compared in 23 patients. In 13 patients, dithranol was applied on both the treatment sides in addition according to the modified Ingram regimen. In 20 patients, NBUVB was found to be significantly more efficacious. Exposure times were comparable between the groups.[37] In a recent randomized comparative study, both the modalities were found to be comparable, 56% in the NBUVB group compared with 40% in the SUV group had clearance, with a median number of exposures of 28.4 for NBUVB and 30.4 for SUV.[38] Given the risk estimates according to the human photocarcinogenesis action spectrum, NBUVB is expected to be 50% more carcinogenic than SUV in equi-erythemogenic doses. Based on these facts, the authors concluded that SUV may be a safer option than NBUVB in the treatment of psoriasis.[38]

NBUVB VS PUVA IN PSORIASIS

After its introduction in the management of psoriasis, the efficacy of NBUVB in clearing disease and duration of remission has been compared with PUVA.

van Weelden *et al*.[39] in a side-to-side comparative study assessed the therapeutic efficacy of PUVA with NBUVB in 10 patients. In three cases, PUVA gave a better result than NBUVB, in 2 cases NBUVB was better than PUVA and in the remaining five cases, there was no difference. Thus, on average, no significant difference was found between the overall therapeutic effectiveness of NBUVB and PUVA.

In an open, non-randomized, intra-individually controlled paired comparison study in 25 patients, NBUVB was found to be as effective as PUVA, but PUVA gave better results in patients with high PASI scores. The overall reduction in PASI was 84% in the NBUVB group and 89% in the PUVA group.[40]

In an open, randomized, controlled study of 54 patients by Markham *et al*.,[41] 29 received NBUVB (three-times a week) and 25 received oral PUVA (twice weekly). Those in the PUVA group required significantly fewer treatments for clearance. There was no significant difference in the number of days to clear or number of days in remission.

In a study involving 100 patients, Gordon *et al*.[42] observed significantly better results with PUVA (PUVA = 49, NBUVB = 51). In the PUVA group, 84% had clearance of lesions with a mean 16.7 exposures while the corresponding figures in the NBUVB group were 63% and 25.3. This study also reported almost three-times the remission rate at 6 months for PUVA than for NBUVB; only 12% of those treated with NBUVB were clear of psoriasis 6 months after treatment compared with 35% of those treated with PUVA. In other studies, treatment with PUVA has been shown to induce remission of 4–6 months or even longer. Thus, compared with PUVA, one of the greatest disadvantages of NBUVB could be its short remission period.

In a double-blind, placebo-controlled trial, Yones *et al*.[43] observed significantly better results with PUVA. Of the 93 patients analyzed, 46 and 47 patients received PUVA and NBUVB, respectively. In the former group, 84% patients achieved clearance after 17 exposures while the corresponding figures in the NBUVB group were 65% and 28.5 exposures. At 6 months post-treatment, 68% and 35% patients in the corresponding groups were in remission. In a study from India, Kaur *et al*.[44] found complete clearance of the lesions in 75% of the patients in the PUVA group (n = 16) and 64% in the NBUVB group (n = 17).

Overall, it appears that both the modalities induce comparable clearance in psoriasis. However, duration of remission may be longer with PUVA. In a recently published retrospective study, it was observed that the duration of remission with PUVA was 386 days on an average compared with 298 days with NBUVB. Although the difference in the duration of remission

was not statistically significant as a trend, patients treated with PUVA remained clear for a period of about 88 days longer than that of patients treated with NBUVB.[45]

Certain advantages of NBUVB, like no or minimal risk of carcinogenesis compared with PUVA, safety of its use in children and pregnant patients, devoid of drug-related (psoralens) side-effects and no requirement of post-treatment eye protection, put it on a better pedestal while considering phototherapy for psoriasis.

COMBINATION REGIMEN WITH NBUVB

NBUVB has been used in combination with topical or systemic anti-psoriatic agents as well as biological agents. Combination therapy has practical benefits: rapid response to treatment and cumulative dose of either drug used in combination is reduced thus effectively reducing the side-effects of both.

The role of topical corticosteroids in conjunction with UVB has been controversial.[46] Earlier reports suggested a fast clearance of disease in patients treated with this combination. A subsequent study has suggested an increased relapse rate.[47] Efficacy of topical dithranol in combination with NBUVB has been assessed by Carrozza *et al*.,[48] and it was observed that the combination resulted in a significant decrease in disease severity. The cumulative UV dose was similar or lower to that found for NBUVB alone.

Studies evaluating efficacy of the combination of calcipotriol and NBUVB have yielded variable results. Woo and McKenna observed that calcipotriol has UVB-sparing effects when this combination is used.[49] Rim *et al*.[50] observed more rapid clearance of psoriasis with combination regimen at the early stage while the final and total cumulative dose of NBUVB in the combination group was slightly lower, although not statistically significant. Messer *et al*.[51] concluded that NBUVB in combination with pre-treatment tacalcitol is superior to either monotherapy alone. Over a 21-days treatment period, the combination regimen led to >50% reduction in PASI in 86% of the lesions while in a side-to-side comparison study tacalcitol monotherapy led to a similar improvement in 38% of the lesions.[51] In contrast, Brands *et al*.[52] observed that addition of calcipotriol to low-dose NBUVB does not have any added therapeutic benefit. It is known that NBUVB can degrade vitamin D3 analogues and thus when used in combination, application of vitamin D3 analogues should follow phototherapy.[53] However, Adachi *et al*.[54] did not observe such deleterious effect of PUVA or NBUVB on vitamin D3 analogues.

The combination of NBUVB with either calcitriol or dithranol has been found to be equally effective. However, patients preferred calcitriol over dithranol when quality of life or treatment acceptability were assessed.[55] Behrens *et al*.[56] observed that addition of topical tazarotene once a day resulted in significantly lower PASI in the treated areas compared with areas receiving NBUVB alone. They concluded that the addition of tazarotene to NBUVB phototherapy promotes more effective, faster clearance of psoriasis compared with NBUVB monotherapy. However, as tazarotene can lead to enhanced susceptibility to burning after phototherapy, a reduction in the dose of NBUVB should be considered. The combination of NBUVB with either calcipotriol or tazarotene yielded comparable results in one study.[57]

Psoralen, both topical and systemic, has been found to enhance the efficacy of NBUVB in treating psoriasis. In a side-to-side comparison of NBUVB vs. combination of NBUVB and psoralen (PUVB) involving 10 patients, lesions cleared earlier in the PUVB-treated side in eight of the nine patients who completed the study.[58] In a subsequent study from the same center involving 100 patients, it was concluded that PUVB is as effective as PUVA. The median number of exposures for clearance was 16.5 for PUVA and 15 for PUVB. The incidence of erythema was comparable.[59] Seckin *et al*.[60] found the beneficial role of topical 8-methoxypsoralen in combination with NBUVB as well. The combination led to greater and earlier improvement than NBUVB alone. The overall clearance rate was also higher in the combination side. However, side-effects were more common in the combination side, pigmentation being the most common.

The combination of methotrexate 15 mg/week and NBUVB was found to be more effective than NBUVB alone. In a randomized, placebo-controlled study by Asawanonda *et al*.,[61] methotrexate (15 mg/week) or placebo was given for 3 weeks before standard NBUVB was started. It was observed that the median time for clearance in the combination group was 4 weeks, which was significantly shorter than that in the NBUVB monotherapy group. A comparative study of sequential cyclosporine and NBUVB vs. NBUVB

treatment alone has indicated that the former is better in the management of psoriasis in terms of lower NBUVB dosage and exposure as well as quick relief of itching.[62] However, these sequential combinations of NBUVB with cytotoxic drugs may not be safe due to the augmented risk of skin carcinogenicity. The combination of acitretin and NBUVB was found to be effective even in difficult-to-treat psoriasis. Forty patients who did not improve with either BBUVB, NBUVB, acitretin monotherapy or combination of BBUVB and acitretin, were treated with a combination of acitretin (25 mg/day) and NBUVB. More than 75% improvement was noticed in 72.5% patients while only 12.5% patients had less than 50% improvement.[63] The combination of acitretin and NBUVB is beneficial as reduced doses of each therapy minimizes their cumulative toxicity. Moreover, acitretin can mitigate the carcinogenic potential of NBUVB.

It was found that thrice-weekly NBUVB in the first 4 weeks of the 6-months treatment schedule of efalizumab, 1 mg/kg/week imparts an achievement of PASI 75 in 70% of the patients. Published reports suggest that only 22–39% patients receiving efalizumab monotherapy achieve PASI 75.[64] Similarly, the combination of NBUVB thrice a week and efalizumab 1 mg/kg/week achieved PASI 75 in 65% of the patients after 12 weeks of treatment.[65] The etanercept and NBUVB combination is also found to have a synergistic effect. In a study where NBUVB thrice-a-week was combined with etanercept 50 mg twice-a-week, PASI 75 was achieved in 84.9% of the patients and PASI 100 was achieved in 26% of the patients.[66] Scheinfeld reported two treatment-resistant cases of psoriasis not responding to methotrexate and UVB alone who responded to the combination of alefacept followed by NBUVB leading to complete clearance of disease.[67]

PRE-TREATMENT EMOLLIENT APPLICATION

Studies on pre-treatment application of emollients before BBUVB had shown that it can rapidly clear psoriasis. Subsequently, similar studies were undertaken in case of NBUVB also. Optimal result of phototherapy in psoriasis requires that it should penetrate sufficiently into the skin. The problem in psoriasis lies in the fact that psoriatic scales form multiple air–corneocyte interfaces that increase reflectance of the optic radiations. Application of a suitable emollient can effectively reduce these air–corneocyte interfaces, thus enhancing transmission of UV radiation through the epidermis. However, every emollient is not suitable for pre-treatment application, i.e. salicylic acid-containing agents like dithranol, coal tar, etc., as they impart a photoprotective effect. The most suitable emollients are those that are non-photosensitizing and non-UV absorbing, and the monochromatic protection factor of such emollients should be <1.2 to avoid a reduction in UV transmission. Several emollients like vaseline oil,[68] glycerine,[69] mineral oil,[70] 5% oleic acid,[71] etc. have been shown to decrease the total cumulative dose and number of exposures required for expected clearance of psoriasis. This has positive implication as the carcinogenic or other cumulative dose-dependent side-effects of NBUVB can be minimized. However, pre-treatment application of coconut oil was not found to accelerate psoriasis clearance.[72] Maximal irradiation regimen was already in place in this study and thus there was no further benefit even with the application of a suitable emollient.

RECENT DEVELOPMENTS

The main drawback of any sort of phototherapy in whole-body chambers or phototherapy panels is the unnecessary exposure of the unaffected normal skin areas that stand as innocent bystanders. This also prevents the use of higher doses of phototherapy, particularly in resistant lesions of psoriasis, so as to achieve rapid clearance of disease. The other drawbacks of the conventional NBUVB chambers are lengthy individual treatment sessions, frequent clinic visits, large space required to accommodate them and intimidation of young patients with shear size and closed chambers.[73] Targeted phototherapy has been developed to treat localized disease (<10% body surface area) keeping these drawbacks of conventional phototherapy in mind. It is known that psoriatic plaques can tolerate higher fluences compared with normal skin; thus, rapid clearance can be achieved.[74] Moreover, as the output is higher from these devices, higher dose can be delivered in a shorter time. Targeted phototherapy may use intense pulse light, excimer laser, photodynamic therapy and UV light-based source for use in varied indications. The source of UV light in these targeted phototherapy devices is similar to the conventional one. However, the light is delivered directly onto the lesions by fiber optic cables. Asawanonda *et al*.[75] in their study of 13 patients, observed that the more the fluence of UVB, the more number of lesions were cleared. Relapse

was however rapid and most of the lesions returned to the pre-treatment state within 4 weeks. Adverse effects noted were asymptomatic erythema and hyperpigmentation in some patients. They concluded that this form of treatment may be of great benefit to patients who have localized, recalcitrant disease that failed to respond to other treatments. As penetration of NBUVB is rather superficial, targeted NBUVB may not be an appropriate option for palmoplantar lesions or nail psoriasis. On the contrary, Campolmi *et al*.[76] observed that palmoplantar lesions respond better and the time to relapse was longer for palmoplantar lesions compared with other areas. Targeted NBUVB (dose applied at four-times MED) in combination with topical 0.1% 8-methoxypsoralen cream has been found to be much more efficacious in clearing psoriatic lesions compared with targeted phototherapy alone.[77,78]

CONCLUSIONS

NBUVB has been found to be a comparatively effective and relatively safer alternative to PUVA in more than two decades of use in the management of psoriasis. Although NBUVB acts as a bridge between topical and systemic immunosuppressive options, it can be used in combination with either of them. The exact dosimetry of NBUVB is yet to be determined; the commonly employed dose regimen is 70% MED as starting dose with 20% dose increments till minimal perceptible erythema is elicited. Far-erythemogenic doses and lower dose increments have also been tried and found to be effective with marginally increased number of exposures for comparable clinical response. The recent development of targeted phototherapy has the prospect of clearing even resistant psoriatic lesions in a shorter period of time.

REFERENCES

1. Goekerman WH. The treatment of psoriasis. Northwest Med 1925;24:229-31.
2. Wiskemann A. UVB- phototherapie der psoriasis mit einer fur die PUVA- therapie entwickelten stehbox. Z Hautzkr 1978;53:633-36.
3. Fischer T. Comparative treatment of psoriasis with UV- lght, trioxsalen plus UV- light and coal tar plus UV- light. Acta Derm Venereol (Stockh) 1977;57:345-50.
4. Parrish JA, Jaenicke KF. Action spectrum for phototherapy of psoriasis. J Invest Dermatol 1981;76:359-62.
5. van Weelden H, De La Faille HB, Young E, van der Leun JC. A new development in UVB phototherapy for psoriasis. Br J Dermatol 1988;119:11-9.
6. Green C, Ferguson J, Lakshmipathi T, Johnson BE. 311 nm UVB phtotherapy- an effective treatment for psoriasis. Br J Dermatol 1988;119:691-96.
7. Honigsmann H, Ortel B. Phototherapy and photochemotherapy. In: Photodermatology. Hawk JL, editor. Arnold London; 1999. p. 223-40.
8. Piskin G, Tursen U, Sylva- Steenland RM, Bos JD, Teunissen MB. Clinical improvement in chronic- plaque type psoriasis lesions after narrow-band UVB therapy is accompanied by a decrease in the expression of IFN- gamma inducers-IL-12, IL-18, and IL-23. Exp Dermatol 2004;13:764-72.
9. Ozawa M, Ferenczi K, Kikuchi T, Cardinale I, Austin LM, Coven TR, *et al*. 312-nanometer ultraviolet B light (narrow- band UVB) induces apoptosis of T cells within psoriatic lesions. J Exp Med 1999;189:711-8.
10. Nickoloff BJ. Cracking the cytokine code in psoriasis. Nat Med 2007;13:242-4.
11. Taylor DK, Anstey AV, Coleman AJ, Diffey BL, Farr PM, Ferguson J, *et al*. Guidelines for dosimetry and calibration in ultraviolet radiation therapy: a report of British photodermatology group workshop. Br J Dermatol 2002;146:755-63.
12. Hofer A, Fink-Puches R, Kerl H, Wolf P. Comparison of phototherapy with near vs far erythemogenic doses of narrow-band ultraviolet B in patients with psoriasis. Br J Dermatol 1998;138:96-100.
13. Kleinpenning MM, Smits T, Boezeman J, van de Kerkhof PC, Evers AW, Gerritsen MJ. Narrowband ultraviolet B therapy in psoriasis: randomized double blind comparison of high- dose and low- dose regimens. Br J Dermatol 2009;161:1351-56.
14. Pai GS, Vinod V, Krishna V. MED estimation for narrowband UV-B on type 4 and type 5 skin in India. Indian J Dermatol Venereol Leprol 2002;68:140-41.
15. Serish, Srinivas CR. Minimal erythema dose (MED) to narrowband ultraviolet- B (NBUVB) and broadband ultraviolet-B (BBUVB)- A pilot study. Indian J Dermatol Venereol Leprol 2002;68:63-4.
16. Tejasvi T, Sharma VK, Kaur J. Determination of minimal erythema dose for narrow band- ultraviolet B radiation in north Indian patients: comparison of visual and Dermaspectrometer readings. Indian J Dermatol Venereol Leprol 2007;73:97-99.
17. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, *et al*. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol 2009;62:114-35.
18. Honigsmann H, Krutmann J. Practical guidelines for broadband UVB, narrowband UVB, UVA-1 phototherapy, and PUVA photochemotherapy- A proposal. In: Dermatological phototherapy and photodiagnostic methods. Krutmann J, Honigsmann H, Clements A, Bergstresser P, editors. New York; Springer; 2001. p. 371.
19. Wainwright NJ, Dawe RS, Ferguson J. Narrowband ultraviolet B (TL-01) phototherapy for psoriasis: which incremental regimen? Br J Dermatol 1998;139:410-4.
20. Boztepe G, Akinci H, Sahin S, Karaduman A, Ersoy Evans S, Erkin G, *et al*. In search of an optimal dose escalation for narrowband UVB phototherapy: Is it time to quit 20% dose increments? J Am Acad Dermatol 2006;55:269-71.
21. An appraisal of narrowband (TL-01) UVB phototherapy. British Photoderamtology Group Workshop report. Br J Dermatol 1997;137:327-30.
22. Dawe RS. A quantitative review of studies comparing the efficacy of narrow-band and broad-band ultraviolet B for psoriasis. Br J Dermatol 2003;149:669-72.
23. Leenutaphong V, Nimkulrat P, Sudtim S. Comparison of phototherapy two times and four times a week with low doses of narrow-band ultraviolet B in Asian patients with psoriasis. Photodermatol Photoimmunol Photomed 2000;16:202-6.
24. Collins P, Wainwright NJ, Amorim I, Lakshmipathi T, Ferguson J. 8-MOP PUVA for psoriasis: A comparison of a minimal phototoxic dose-based regimen with a skin-type approach. Br J Dermatol 1996;135:248-54.
25. Boztepe G, Karaduman A, Sahin S, Hayran M, Holemen F. The

effect of maintenance narrow-band ultraviolet B therapy on the duration of remission for psoriasis: A prospective randomized clinical trial. Int J Dermatol 2006;45:245-50.
26. Ibbotson SH, Bilsland D, Cox NH, Dawe RS, Diffey B, Edwards C, *et al*. An update and guidance on nrrowband ultraviolet B phototherapy: A British Photodermatology Group Workshop report. Br J Dermatol 2004;151:283-97.
27. George SA, Ferguson J. Lesional blistering following narrow-band (TL-01) UVB phototherapy for psoriasis: A report of four cases. Br J Dermatol 1992;127:445-6.
28. Calzavara- Pinton PG, Zane C, Candiago E, Facchetti F. Blisters on psoriatic lesions treated with TL-01 lamps. Dermatology 2000;200:115-9.
29. Jo SJ, Yoon HS, Woo SM, Youn JI. Time course of tanning induced by narrow-band UVB phototherapy in Korean psoriasis patients. Photodermatol Photoimmunol Photomed 2006;22:193-9.
30. Young A. Carcinogenicity of UVB phototherapy assessed. Lancet 1995;345:1431-2.
31. Man I, Crombie IK, Dawe RS, Ibbotson SH, Ferguson J. The photocarcinogenic risk of narrowband UVB (TL-01) phototherapy: Early follow- up data. Br J Dermatol 2005;152:755-57.
32. Weischer M, Blum A, Eberhard F, Rocken M, Berneburg M. No evidence for increased skin cancer risk in psoriasis patients treated with broadband or narrowband phototherapy: A first retrospective study. Acta Derm Venereol 2004;84:370-4.
33. Lee E, Koo J, Berger T. UVB phototherapy and skin cancer risk: a review of the literature. Int J Dermatol 2005;44:355-60.
34. Coven TR, Burack LH, Gilleaudeau R, Keogh M, Ozawa M, Krueger JG. Narrow band UV-B produces superior clinical and histopathological resolution of moderate to severe psoriasis compared with broadband UVB. Arch Dermatol 1997;133: 1514-22.
35. Bandow GD, Koo JY. Narrow-band ultraviolet B radiation: a review of the current literature. Int J Dermatol 2004;43:555-61.
36. Karvonen J, Kokkonen EL, Ruotsalainen E. 311 nm UVB lamps in the treatment of psoriasis with the Ingram regimen. Acta Derm Venereol 1989;69:82-5.
37. Storbeck K, Holzle E, Schurer N, Lehmann P, Plewig G. Narrow-band UVB (311 nm) versus conventional broad-band UVB with and without dithranol in phototherapy for psoriasis. J Am Acad Dermatol 1993;28:227-31.
38. Kirke SM, Lowder S, Lloyd JJ, Diffey BL, Matthews JN, Farr PM. A randomized comparison of selective broadband UVB and narrowband UVB in the treatment of psoriasis. J Invest Dermatol 2007;127:1641-46.
39. van Weelden H, Baart De La Faille H, Young E, van der Leun JC. Comparison of narrow-band UV-B phototherapy and PUVA photochemotherapy (PUVA) in the treatment of psoriasis. Acta Derm Venereol (Stockh) 1990;70:212-5.
40. Tanew A, Ortel B, Honigsmann H. Half-side comparison of erythemogenic versus suberythemogenic UVA doses in oral photochemotherapy of psoriasis. J Am Acad Dermatol 1999;41:408-13.
41. Markham T, Rogers S, Collins P. Narrow band UVB (TL-01) phototherapy vs. 8-methoxypsoralen Psoralen-UV-A for the treatment of chronic plaque psoriasis. Arch Dermatol 2003;139:325-8.
42. Gordon PM, Diffey BL, Matthews JN, Farr PM. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999;41:728-32.
43. Yones SS, Palmer RA, Garibaldinos TT, Hawk JL. Randomized double- blind trial of the treatment of chronic- plaque psoriasis: efficacy of psoralen- UV-A therapy Vs narrowband UV- B therapy. Arch Dermatol 2006;142:836-42.
44. Kaur J, Shrama VK, Sethuraman G, Tejasvi T. Comparison of the efficacy of psoralen ultraviolet A with narrowband ultraviolet B phototherapy for the treatment of chronic plaque psoriasis in patients with skin types 4 and 5. Clin Exp Dermatol 2008;33:513-515.
45. Brazzelli V, Barbagallo T, Trevisan V, Muzio F, De Silvestri A, Borroni G. The duration of clinical remission of photochemotherapy and narrow-band UV-B phototherapy in the treatment of psoriasis: a retrospective study. Int J Immunopathol Pharmacol. 2008;21:481-4.
46. Lidbrink P, Johannesson A, Hammar H. Psoriasis treatment: faster clearance when UVB-dithranol is combined with top-ical clobetasol propionate. Dermatologica 1986;172:164-8.
47. Dover JS, McEvoy MT, Rosen CF, Arndt KA, Stern RS. Are topical corticosteroids useful in phototherapy for psoriasis? J Am Acad Dermatol 1989;20:748-54.
48. Carrozza P, Hausermann P, Nestle FO ,Burg G, Boni R. Clinical efficacy of narrow-band UVB (311 nm) combined with dithranol in psoriasis. An open pilot study. Dermatology 2000;200:35-9.
49. Woo WK, McKenna KE. Combination TL01 ultraviolet B phototherapy and topical calcipotriol for psoriasis: A prospective randomized placebo-controlled clinical trial.Br J Dermatol 2003;149:146-50.
50. Rim JH, Choe YB, Youn JI. Positive effect of using calcipotriol ointment with narrow-band ultraviolet B phototherapy in psoriatic patients. Photodermatol Photoimmunol Photomed 2002;18:131-4.
51. Messer G, Degitz K, Plewig G, Rocken M. Pretreatment of psoriasis with vitamin D3 derivative tacalcitol increases the responsiveness to 311-nmultraviolet B: Results of a controlled, right/left study. Br J Dermatol 2001;144:628-9.
52. Brands S, Brakman M, Bos JD, de Rie MA. No additional effect of calcipotriol ointment on low-dose narrow-band UVB phototherapy in psoriasis. J Am Acad Dermatol 1999;41:991-5.
53. Lebwohl M, Quijije J, Gilliard J, Rollin T, Watts O. Topical calcitriol is degraded by ultraviolet light. J Invest Dermatol 2003;121:594-5.
54. Adachi Y, Uchida N, Matsuo T, Horio T. Clinical effect of vitamin D3 analogues is not inactivated by subsequent UV exposure. Photodermatol Photoimmunol Photomed 2008;24:16-8.
55. Hofmann UB, Eggert AA, Brocker EB, Goebeler M. Calcitriol vs. dithranol in combination with narrow-band ultraviolet B (311 nm) in psoriasis. Br J Dermatol 2003;148:779-83.
56. Behrens S, Grundmann- Kollmann M, Schiener R, Peter RU, Kerscher M. Combination phototherapy of psoriasis with narrow-band UVB irradiation and topical tazarotene gel. J Am Acad Dermatol 2000;42:493-5.
57. Schiener R, Behrens-Williams SC, Pillekamp H, Kaskel P, Peter RU, Kerscher M. Calcipotriol vs. tazarotene as combination therapy with narrowband ultraviolet B (311 nm): Efficacy in patients with severe psoriasis.Br J Dermatol 2000;143:1275-8.
58. Sakuntabhai A, Diffey BL, Farr PM. Response of psoriasis to psoralen- UVB photochemotherapy. Br J Dermatol 1993;128:296-300.
59. de Berker DA, Sakuntabhai A, Diffey BL, Matthews JN, Farr PM. Comparison of psoralen- UVB and psoralen- UVA photochemotherapy in the treatment of psoriasis. Arch Dermatol 1997;36:577-81.
60. Seckin D, Usta I, Yazici Z, Senol A. Topical 8- methoxypsoralen increases the efficacy of narrowband ultraviolet B in psoriasis. Photodermatol Photoimmunol Photomed 2009;25:237-41.
61. Asawanonda P, Nateetongrungsak Y. Methotrexate plus narrowband UVB phototherapy versus narrowband UVB phototherapy alone in the treatment of plaque-type psoriasis: a randomized, placebo-controlled study. J Am Acad Dermatol 2006;54:1013-8.
62. Calzavara- Pinton P, Leone G, Venturini M, Sala R, Colombo D, La Parola IL, *et al*. A comparative non randomized study of narrow-band (NB) (312 ± 2 nm) UVB phototherapy versus sequential therapy with oral administration of low-dose Cyclosporin A and NB-UVB phototherapy in patients with severe psoriasis vulgaris. Eur J Dermatol 2005;15:470-3.
63. Spuls PI, Rozenblit M, Lebwohl M. Retrospective study of the

efficacy of narrowband UVB and acitretin. J Dermatolog Treat 2003;14:17-20.
64. Zane C, Capezzera R, Venturini M, Sala R, Facchinetti E, Pedretti A, *et al*. A short cycle of narrow-band UVB phototherapy in the early phase of long-term efalizumab can provide a quicker remission of moderate and severe psoriasis: A pilot study. Dermatology 2009;218:321-6.
65. Kircik LH, Liu C, Goffe BS. Treatment of moderate to severe plaque psoriasis with concomitant efalizumab and narrow-band ultraviolet B phototherapy. J Drugs Dermatol 2008;7: 947-52.
66. Kircik L, Bagel J, Korman N, Menter A, Elmets CA, Koo J, *et al*. Unite Study Group. Utilization of narrow-band ultraviolet light B therapy and etanercept for the treatment of psoriasis (UNITE): Efficacy, safety, and patient-reported outcomes. J Drugs Dermatol 2008;7:245-53.
67. Scheinfeld N. Therapy-resistant psoriasis treated with alefacept and subsequent narrow band ultraviolet B phototherapy with total clearing of psoriasis. Dermatol Online J 2005;11:7.
68. Penven K, Leroy D, Verneuil L, Faguer K, Dompmartin A. Evaluation of Vaseline oil applied prior to UVB TL01 phototherapy in the treatment of psoriasis. Photodermatol Photoimmunol Photomed 2005;21:138-41.
69. Fetil E, Akarsu S, Ilknur T, Kusku E, Gunes AT. Effects of some emollients on the transmission of ultraviolet. Photoermatol Photoimmunol Photomed 2006;22:137-40.
70. Jain VK, Bansal A, Aggarwal K, Jain K. Enhanced response of childhood psoriasis to narrow-band UV-B phototherapy with pre-irradiation use of mineral oil. Pediatr Dermatol 2008;25:559-64.
71. Martín-Ezquerra G, Sánchez-Regaña M, Umbert-Millet P. Optimization of narrow-band uvb with a 5% oleic acid cream in the treatment of Psoriasis. J Drugs Dermatol 2007;6:290-2.
72. George SA, Bilsland DJ, Wainwright NJ, Ferguson J. Failure of coconut oil to accelerate psoriasis clearance in narrow-band UVB phototherapy or photochemotherapy. Br J Dermatol 1993;128:301-5.
73. Mysore V. Targeted phototherapy. Indian J Dermatol Venereol Leprol 2009;75:119-25.
74. Speight EL, Farr PM. Erythemal and therapeutic response of psoriasis to PUVA using high-dose UVA. Br J Dermatol 1994;131:667-72.
75. Asawanonda P, Chingchai A, Torranin P. Targeted UV-B phototherapy for plaque-type psoriasis. Arch Dermatol 2005;141:1542-6.
76. Lotti T, Rossi R, Campolmi P. Targeted UV-B phototherapy: When and why to start. Arch Dermatol 2006;142:933-34.
77. Amornpinyokeit N, Asawanonda P. 8-Methoxypsoralen cream plus targeted narrowband ultraviolet B for psoriasis. Photodermatol Photoimmunol Photomed 2006;22:285-9.
78. Asawanonda P, Amornpinyokeit N, Nimnuan C. Topical 8-methoxypsoralen enhances the therapeutic results of targeted narrowband ultraviolet B phototherapy for plaque-type psoriasis. J Eur Acad Dermatol Venereol 2008;22:50-5.

ADDENDUM

Since this manuscript was submitted to the journal, following studies have got recently published on NBUVB treatment for psoriasis. A brief recount is given below for an update.

In Iranian patients, no statistical difference was found between 3-times a week Vs. 5-times a week groups in terms of percentage of patients who achieved clearance, number of treatments, cumulative UVB dose, and incidence of side effects. More rapid clearance of psoriasis was, however, observed in the 5-times a week treatment group.[1]

In a study from North India, NBUVB and PUVA were found to be equally efficacious for treatment of chronic plaque psoriasis. Marked improvement was observed in 81.8% and 80.9% patients respectively. In those patients having follow-up data at 6 months, 42.8% and 26.7% patients were still in remission ($p>0.05$),[2] In dark- skinned Saudi Arabian patients also, NBUVB has been found to be safe and effective. The treatment response was found to be better particularly in female patients.[3]

Synchronous balneophototherapy (bathing in Dead Sea salt solution plus NBUVB) have been found to be more effective than NBUVB alone after 35 treatments and 6 months follow- up.[4] The combination of methotrexate and NBUVB has been found superior to NBUVB alone in another study considering rate of PASI75 achievement. Number of treatment sessions and number of weeks of treatment as well as total cumulative dose of NBUVB was significantly lower in the combination group. Post- treatment incidence of relapse was comparable between the groups in 12-week follow up.[5]

Regular visit to the phototherapy clinic may not be possible or convenient for patients. In a recent study, home based NBUVB phototherapy was found comparable to clinic based phototherapy considering treatment response and cost of treatment. The authors concluded that if possible, home phototherapy should be the primary treatment option as patients prefer being treated at their home.[6]

REFERENCES

1. Hallaji Z, Barzegari M, Balighi K, Mansoori P, Taheri A, Mansoori P. A comparison of three times vs. five times weekly narrowband ultraviolet B phototherapy for the treatment of chronic plaque psoriasis. Photodermatol Photoimmunol Photomed. 2010;26:10-5.
2. Chauhan PS, Kaur I, Dogra S, De D, Kanwar AJ. Narrowband ultraviolet B versus psoralen plus ultraviolet A therapy for severe plaque psoriasis: an Indian perspective. Clin Exp Dermatol. 10.1111/j.1365-2230.2010.03874.x
3. Al Robaee AA. The usefulness of narrowband UVB as a monotherapy for the treatment of chronic plaque psoriasis. J Drugs Dermatol. 2010;9:989-91.
4. Klein A, Schiffner R, Schiffner-Rohe J, Einsele-Krämer B, Heinlin J, Stolz W,et al. A randomized clinical trial in psoriasis: synchronous balneophototherapy with bathing in Dead Sea salt solution plus narrowband UVB vs. narrowband UVB alone (TOMESA-study group). J Eur Acad Dermatol Venereol. doi: 10.1111/j.1468-3083.2010.03840.x.
5. Mahajan R, Kaur I, Kanwar AJ. Methotrexate/narrowband UVB phototherapy combination vs. narrowband UVB phototherapy in the treatment of chronic plaque-type psoriasis–a randomized single-blinded placebo-controlled study. J Eur Acad Dermatol Venereol 2010;24:595-600.
6. Koek MB, Sigurdsson V, van Weelden H, Steegmans PH, Bruijnzeel-Koomen CA, Buskens E. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). BMJ. doi: 10.1136/bmj.c1490.