NARROW BAND ULTRAVIOLET B (NB-UVB) "PHOTOTHERAPY" Review Of Literature (Part One)

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Narrow Band UVB (311nm)
Review Of Literature:

Contents Of Part One:

Contents Of Part Two:

Introduction:

This review is started by a brief general introduction about photobiology, followed by review of most of what was published about narrow band ultraviolet B (NB-UVB) in the medical literature in the past decade.

Reviewing the literature was done with the help of physician silver platter Dermatology medline that covers the period between 1966 and Dec.2000. we selected medline in our work because all internationally accepted journals and publications are almost included in this computerized facility.

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Narrow Band Ultraviolet B
NB-UVB (311nm)

Photobiology
Definition:

Photobiology is the study of the effects of ultraviolet (UV) and visible radiation on living matter. Cutaneous (dermatological) photobiology is concerned with those effects on skin[1].

UV and visible radiation, which comprises a very small part of the electromagnetic radiation spectrum.

Electromagnetic radiation is energy released during the transition of a molecular electron from a higher energy, outer molecular orbital to a less energetic, inner one. Each such emission, known as a photon, is a discrete, oscillating, electromagnetic pulse of energy, (joules, J), wavelength, lamda (nanometres, nm, 10 -10 m) and velocity through space, C (3 ∞ 108 m/sec), such that E= hc/ lamda where h = 6.63∞10-34 J.sec (Planck's constant)

Approximate emission spectra of typical sources encountered in dermatological photobiology and elsewhere, with action spectrum for human cutaneous erythema for comparison.

Sunlight has profound effects on the skin and is associated with a variety of diseases. Ultraviolet light causes most photobiologic skin reactions and diseases. The accepted unit for measuring the wavelength of light is the nanometer (nm). The solar radiation reaching the earth is a continuous spectrum consisting of wavelengths of electromagnetic energy above 290 nm [2].

By convention, ultraviolet light is divided into UVA (320 to 400 nm; long wave, black light), UVB (290 to 320 nm; middle wave, sunburn), and UVC (100 to 290 nm; short wave, germicidal) [2].

UVA causes immediate and delayed tanning

and contributes little to erythema and burning. It is constant throughout the day. The longer wavelengths of UVA can penetrate more deeply, reaching the dermis and subcutaneous fat. Chronic exposure to UVA radiation causes the connective tissue degeneration seen in photoaging. UVA augments the carcinogenic effects of UVB. UVA penetrates window glass and interacts with topical and systemic chemicals and medication [2].

UVB delivers a high amount of energy to the stratum corneum and superficial layers of the epidermis and is primarily responsible for sunburn, suntan, and skin cancers. It produces tanning more efficiently than UVA. It is most intense when the sun is directly overhead between 10 a.m. and 2 p.m. UVB is absorbed by window glass. Prior exposure to UVA enhances the sunburn reaction from UVB [2].

UVC is almost completely absorbed by the ozone layer and is only transmitted by artificial sources such as germicidal lamps and mercury arc lamps [2].

Three types of phototherapy and 2 forms of photochemotherapy are now available for treatment of more than 40 diseases of the skin. Broadband ultraviolet B (UVB) phototherapy and oral psoralen photochemotherapy (PUVA) therapy are most widely available while there has been increased interest in topical PUVA therapy. Narrow-band UVB (NB-UVB) phototherapy and UVA-1 phototherapy offer potential for the future [3].

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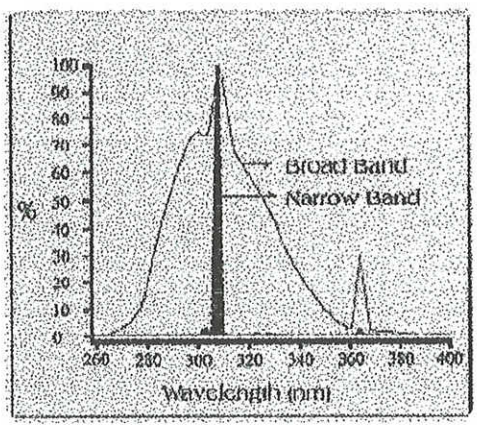

Conventional broad band UVB lamps emit a variety of wavelengths ranging from 280-330 nm[4].

Clinical studies show the peak therapeutic effectiveness of UVB to be within the range of 295-313 nm, but wavelengths below 300 nm can cause erythma or severe burning and increase the risk of skin cancer[4].

Narrow band UVB virtually eliminates superfluous and harmful UV by emitting only wavelengths of 311-312 nm[4].

Eliminating UV Wavelengths below 311 nm permits higher intensities and longer exposure times so you can derive the maximum benefit from phototherapy[4].

The increased tolerance and effectiveness permits more aggressive treatment regimens, resulting in a shorter course of treatment

Ultraviolet wavelengths around 305-315 nm are most efficient for clearing psoriasis[4].

Erythema of uninvolved skin is a limiting factor for UVB phototherapy in psoriasis. In psoriasis the proliferative compartment and stratum corneum are thicker than that of normal skin[4].

Longer wavelengths are more efficient than shorter ones because of their ability to penetrate deeply into thick psoriatic plaques. (Standard UVB units employ broad band TL-12 type fluorescent tubes, which emit between 280-350 nm, with a narrow peak at 305 nm.)[4].

Varieties of Narrow-Band Phototherapy:

Selective UV Phototherapy (SUP) (295-330nm):

One approach to narrow-band phototherapy - used mostly in Germany - has been the so-called selective UV phototherapy (SUP), which uses the spectrum of a high pressure mercury lamp that has additional emission peaks between 295 and 330 nm [4].

TL-01(304-334nm):

A more recent successful development is the availability of the so-called narrow-band UVB Philips TL-01 fluorescent tube, which employs a phosphur that emits a high, distinct peak at 311-312 nm, with minor spikes at 304 and 334 nm [4].

Narrow-Band Ultraviolet B (NB-UVB) (311nm):

Gradually, both SUP and narrow-band UVB have become loose synonyms for the TL-01 lamp.

Narrow-band, or 311 nm phototherapy has a higher ratio of therapeutic to erythemogenic activity, resulting in increased efficacy, reduced incidence of burning, and longer remissions. However, if the same number of bulbs per box are used, the new system requires twice the irradiation time compared to broad-band tubes, resulting in

more inconvenience to the patient, the technician, and the treatment center. Adding additional bulbs to each treatment cubicle overcomes this problem, but creates problems with additional heat production and an increased need for ventilation systems [4].

Powerful 100 W Bulbs (311 Nm):

Fortunately, new 100 W bulbs, more powerful than the first 311 nm bulbs, allow the phototherapist to deliver narrow-band UVB treatments in irradiation times comparable to those of traditional broad-band UVB.

Treatment regimens for these new bulbs have been modeled on existing broad-band therapies. For example, treatments begin at 70% to 80% of the patient's minimal erythema dose. Schedules range from two and five times per week [4].

Effects of UVB on normal skin

1- BB-UVB

Ultraviolet radiation B (UVB) on the skin induces:

1- erythema,
2- inflammation
3- modifications of the immune system.

These changes have been reported after excessive short-term or long-term exposure to broad spectrum UVB.

2- NB-UVB

Viac-J examined the effects of local repetitive UVB irradiation of 311 nm wavelength on the skin of seven young volunteers. Skin biopsies were taken before and after UVB irradiation. Exposure of NB-UVB 311 nm Induces:

1- A drastic reduction of CD1a+ cells
2- Moderate increase of HLA-DR+ dendritic cells in the epidermis without infiltration by CD11b macrophages.
3- In the dermis, vessel-associated ICAM-1 expression increased
4- And an induction of E-selectin occurred on nearly 20 to 40% of endothelial cells,
5- VCAM-1 expression remained undetectable.
6- The percentage of LFA-1+ cells did not change significantly after irradiation.

These observations may be compatible with a selective role of UVB 311 nm on the skin immune response[5].

What are the indications?

Generally speaking the indications of NB-UVB are almost those of BB-UVB, but because of the safer margin, NB-UVB is considered as a new field opened for many therapeutic trials and it is expected to have an elongating list of indications in the near future.

As in photochemotherapy NB-UVB may be used to treat or to prevent a disease.

Diseases that may benefit from NB-UVB:

1- Psoriasis
2- Eczema
3- Vitiligo
4- Small Plaque Parapsoriasis and early MF
5- Prurigo Nodularis
6- Subcorneal Pustular Dermatosis (Sneddon-Wilkinson Disease)
7- Pruritic folliculitis of pregnancy
8- Pityriasis rubra pilaris

Diseases that may be prevented by NB-UVB:

1- Photodermatosis
2- Hydroa Vacciniforme
3- Erythropoietic Protoporphyria

Therapeutic trials, comparative studies and combination therapy with NB-UVB:

There are also a lot of therapeutic trials comparative studies and combination therapy which will be discussed in part two .

In our clinic:

NB-UVB has been tried successfully, in addition to what was mentioned above, in the treatment of many other diseases. The results will be published after analysing data and results.

These indications are:

1- Piyriasis rosea
2- Pityriasis lichinoides
3- Reactive perforating collagenosis
4- Achromia parasitica
5- Chronic and recurrent infundibulofolliculitis
6- Alopecia areata and alopecia universalis
7- Lichen planus.
8- Lichen nitidus

Diseases that may benefit from NB-UVB:

1- psoriasis

NB UVB(TL01) In Tratment Of Psoriasis:

In 1992 Picot-E reported the results of an open study conducted on 53 patients with psoriasis treated by narrow-band UVB phototherapy, using Philips' TL01 lamp.

With a simple procedure which did not require MED determination, this treatment gave satisfactory results in 92% of the cases, with mild burns in only 9 %.

The morphological type of psoriasis (patchy, guttate or nummular) had no influence on the therapeutic result, but the degree of infiltration of the lesions and their location on the lower limbs proved to be a factor of relative resistance.

In most patients the results were obtained in 20 sessions. with a mean cumulative dose of 20.19 +/- 2.7 J/cm2. Some patients had an additional treatment of 6 sessions[6].

2- Eczema:

NB-UVB can be used effectively in the treatment of childhood or adulthood atopic dermatitis.

I - Phototherapy For Atopic Eczema With Narrow-Band UVB:

Management of atopic dermatitis has been less than satisfactory. Conventional therapy has not been particularly successful, and prolonged use of topical corticosteroids and systemic immunosuppressant drugs (eg, corticosteroids, cyclosporine, azathioprine) can result in severe cutaneous and systemic effects.

Grundmann evaluated the effect of UVB at 311 nm to treat 5 patients with moderate to severe atopic dermatitis. In each patient a mean cumulative dose of 9.2 J/cm2 was applied over a mean of 19 irradiations. Narrow-band UVB notably reduced atopic dermatitis after 3 weeks in all patients [7].

II - Narrow-Band (TL-01) UVB Air-Conditioned Phototherapy For Chronic Severe Adult Atopic Dermatitis:

George-SA tried in an open study on 21 severely affected adult atopic dermatitis patients, in air-conditioned narrow-band UVB phototherapy three times weekly for 12 weeks. This study resulted in a 68% reduction in atopic dermatitis severity scores, with a concomitant 88% reduction in potent topical steroid use.

Follow-up at 24 weeks revealed that six patients had relapsed to > 70% of pre-phototherapy severity scores; the remaining 15 continued to derive long-term benefit. The mean value of potent topical steroid use remained 50% below pre-phototherapy needs.

Narrow-band UVB phototherapy appears an effective, steroid-sparing treatment for chronic severe atopic dermatitis, offering long-term benefits in the majority of those treated [8].

Comment: By combaring George-SA with Grundmann results it could be said that the adult severe atopic dermatitis needs higher doses, longer tratment period, but it results in longer clearance period.

III - Comparison of bath-PUVA versus NB-UVB in severe chronic atopic dermatitis:

In patients with severe chronic atopic dermatitis (AD), both photochemotherapy [psoralen ultraviolet A (PUVA)] and narrow-band (TL-01) UV B phototherapy have been reported to be very effective. As no data exist on the relative therapeutic efficacy of these two regimens, Der-Petrossian-M performed a randomized investigator-blinded half-side comparison study on 12 patients with severe chronic AD. Half-side irradiation with threshold erythemogenic doses of 8-methoxypsoralen bath-PUVA and narrow-band UVB was performed three times weekly over a period of 6 weeks. The severity of the disease was assessed separately for the paired halves of the patients' bodies by a modified SCORAD score at baseline and after 2, 4 and 6 weeks of treatment. Ten of the 12 patients completed the trial. All but one showed marked improvement or complete remission with both treatments. The mean baseline SCORAD score decreased by 65.7% by the bath-PUVA treatment and by 64.1% by the narrow-band UVB treatment (P = 0.48). No serious adverse reactions to either of the two regimens were observed. The author data confirm the high efficacy of bath-PUVA and narrow-band UVB phototherapy in the treatment of patients with chronic severe AD.

Both regimens appear to be equally effective when administered in equi-erythemogenic doses[9].

3- Vitiligo in children :

I -Treatment Of Generalized Vitiligo In Children With Narrow-Band UVB Radiation Therapy:

In an open trial, 51 children (20 males, 31 females) with generalized vitiligo were treated twice weekly with narrow-band UVB radiation therapy for the maximum period of 1 year. The Children's Dermatology Life Quality Index (CDLQI) was used to evaluate the psychosocial. impact of disease and treatment and was scored before and after therapy.

The treatment resulted in more than 75% overall repigmentation in 53% of patients and in stabilization of the disease in 80%.

Responsiveness to therapy was positively correlated with localization of the lesions and the patients' compliance. Adverse events were limited and transient. The

better the repigmentation grade, the better the CDLQI scores had improved.

It was concluded that Narrow-band UVB therapy is effective and safe in childhood vitiligo; it also may significantly improve the quality of life [10].

II -Successful Treatment Of Vitiligo Patients With Narrow-Band UVB:

Njoo observed that the response profile of vitiligo patients to broad-band UVB therapy was found to be comparable with that of NB-UVB [11].

4- Small Plaque Parapsoriasis And Early MF:

Narrowband (311-Nm) UV-B Therapy For Small Plaque Parapsoriasis And Early-Stage Mycosis Fungoides:

Broadband UV-B phototherapy has been used for many years in the treatment of small plaque parapsoriasis (SPP) and early-stage mycosis fungoides (MF).

Hofer et al in 1999 wanted to investigate the effect on these diseases of narrowband (311-nm) UV-B therapy. He found that Narrowband UV-B therapy is an effective short-term treatment modality for clearing SPP and early-stage MF. However, the treatment response did not sustain long-term remission.

Further studies are necessary to examine how the clinical response to and follow-up after narrowband UV-B therapy compares with that of established phototherapy modalities in these diseases [12].

Comment: In our patients when MF is clear maintenance doses are used over long time to maintain the improvement. The aim of maintenance is to reach the menimal effective dose in both frequency and dose per session. This maintenance treatments or schedule results in longer remissin period and lower total cummulative doses.

Later on Clark-C compared the available treatments for patch-stage mycosis fungoides. His conclusion was that TL-01 is an effective, convenient therapy that may have less risk of long-term adverse effects than current alternatives (including BB-UVB, photochemotherapy, topical nitrogen mustards, electron-beam therapy) [13] .

5- Prurigo Nodularis

Sequential combined therapy with thalidomide and narrow-band UVB therapy could improve the management of prurigo nodularis with minimal side effects (for details and reference see therapeutic trials in part two).

6- Subcorneal Pustular Dermatosis (Sneddon-Wilkinson Disease)

Cameron and Orton reported seperately Subcorneal pustular dermatosis (Sneddon-Wilkinson disease) treated with narrowband (TL-01) UVB phototherapy [14,15].

7- Pruritic folliculitis of pregnancy treated with NB-UVB

A letter published in july 1999 by Reed-J about the use of narrowband (TL-01) ultraviolet B phototherapy in the treatment of Pruritic folliculitis of pregnancy [16].

8- Pityriasis rubra pilaris treated with acitretin and NB-UVB:

Kirby-B published in Feb. 2000 a letter about the use of acitretin and narrow-band ultraviolet B (Re-TL-01) in the treatment of Pityriasis rubra pilaris [17].

Diseases that may be prevented by NB-UVB:

Photodermatosis

Narrow-band phototherapy is an effective and preventative treatment for the photodermatoses:

Collins-P et al tried NB-UVB (TL01) in the treatment of twenty patients with photodermatoses for evaluation of this new type of treament :

Actinic prurigo (n = 6), Hydroa vacciniforme (n = 4), Idiopathic solar urticaria (n = 1), Amiodarone-induced photosensitivity (n = 1) and a range of cutaneous porphyrias (n = 8) were treated with a 'hardening' course of narrow-band ultraviolet B (TL-01) phototherapy in springtime. The response to phototherapy was monitored subjectively, by interviewing patients after the summer, and objectively by monochromator phototesting, before and after phototherapy.

Fifteen patients (75%) reported that treatment was worthwhile. Monochromator phototesting after phototherapy revealed a fourfold increase in the minimal erythema dose in those with abnormal photosensitivity to ultraviolet A wavebands.

Adverse effects included: erythema in seven patients (35%), pruritus in five patients (25%) and provocation of the eruption in four patients (20%).

The author routinely consider narrow-band UVB phototherapy for problem photodermatoses [18].

Hydroa Vacciniforme

Hydroa Vacciniforme Treated With Narrow-Band UVB Phototherapy:

In Feb 2000 Gupta-G treated 5 Hydroa vacciniforme patients with narrow-band UVB (TL-01) phototherapy, 3 patients (60%) reported beneficial results with an increase in tolerance to sunlight exposure and associated reduction in disease severity [19].

Erythropoietic Protoporphyria

Erythropoietic protoporphyria treated with narrow-band (TL-01) UVB phototherapy:

Erythropoietic protoporphyria is a rare photodermatosis for which treatment options are limited.

Treatment with narrow-band UVB phototherapy resulted in marked subjective improvement in photosensitivity, which was confirmed by abolition of demonstrated abnormalities on monochromator phototesting[20].

Mechanism of Action Of NB-UVB In Psoriasis

Narrow-Band UVB Induces Apoptosis Of T Cells Within Psoriatic Lesions

Narrow-band ultraviolet B light (UVB) is a new form of therapy for psoriasis, but its mechanism of action is unknown.

In a bilateral comparison clinical study, daily exposure of psoriatic plaques to broad-band UVB (290-320 nm) or 312-nm UVB depleted T cells from the epidermis and dermis of psoriatic lesions. However, 312-nm UVB was significantly more depleting in both tissue compartments.

To characterize the mechanism of T cell depletion, assays for T cell apoptosis were performed on T cells derived from UVB-irradiated skin in vivo and on T cells irradiated in vitro with 312-nm UVB. Apoptosis was induced in T cells exposed to 50-100 mJ/cm2 of 312-nm UVB in vitro, as measured by increased binding of fluorescein isothiocyanate (FITC)-Annexin V to CD3(+) cells and by characteristic cell size/granularity changes measured by cytometry. In vivo exposure of psoriatic skin lesions to 312-nm UVB for 1-2 wk also induced apoptosis in T cells as assessed by the terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) reaction in tissue sections, by binding of FITC-Annexin V to CD3(+) T cells contained in epidermal cell suspensions, and by detection of apoptosis-related size shifts of CD3(+) cells. Induction of T cell apoptosis could be the main mechanism by which 312-nm UVB resolves psoriasis skin lesions[21].

Effects of phototherapy on the production of cytokines by peripheral blood mononuclear cells and on systemic antibody responses in psoriatics:

Exposure to ultraviolet B (UVB) radiation results in the suppression of many cell-mediated immune responses, and recent studies mice and murine cells in vitro suggest a shift from a T-helper 1 (Th1) to a Th2 type of response on irradiation. Active psoriasis is considered to be a Th1-type disorder, chiefly on the basis of the cytokines produced by inflammatory cells in psoriatic lesions.

Jones et al investigated the effect of phototherapy in patients with psoriasis on the cytokine profile of mitogen-stimulated mononuclear cells from peripheral blood and the concentration of IgG subclasses and IgE in the plasma. Eight patients were irradiated with a broad-band UV source (Sylvania UV6; 280-400 nm) three times a week and another eight with a narrow-band UVB source (Philips TL-01; 311-313 nm). Peripheral blood was collected before therapy started and after 1-4 weeks of therapy. Peripheral blood mononuclear cells were stimulated in vitro with phytohemagglutinin; proliferation was measured by incorporation of tritiated thymidine and culture supernatants assayed for interleukin (IL)-2, -4 and -10 and gamma-interferon (IFN) by enzyme-linked immunosorbent assays. Lymphoproliferation was not consistently affected by 4 weeks of UV6 therapy, and there was also no consistent change in the production of IL-2, IL-10 or gamma-IFN. In contrast, 4 weeks of TL-01 therapy significantly suppressed lymphoproliferative responses. In addition the production of IL-2, IL-10 and gamma-IFN was lowered after 1 week of TL-01 therapy, and this was even more apparent after the treatment had been extended to 4 weeks. IL-4 concentrations were below detectable levels in all the samples throughout the study. The amounts of IgG1, -2, -3 and -4 and IgE in the plasma of the patients did not vary with either of the two phototherapies. Thus, although no evidence was obtained to indicate that UV6 exposures affected T-helper subsets in psoriasis, TL-01 inhibited the activity of both Th1 and Th2 subsets while not altering plasma antibody concentrations[22].

What are the contraindications?

On reviewing the literature we could not bind any article about the contraindications of NB-UVB.

This could be because NB-UVB is considered as special form of BB-UVB in relation to indications, contraindications, side effects, but with much safer range of use because of the elemination of superfluous and harmful UV with wave length below 311 nm (see page

2)

What are the advantages of NB UVB?

1- No Systemic Medications:

Narrow Band phototherapy avoids the adverse side effects of the psoralens and other photosesitizers used in conventional PUVA therapy and general photochemotherapy, since UVB treatment requires no supplemental drugs [4] .

NB-UVB is phototherapy and not photochemotherapy unless combined with systemic medication to increase its effect as we will see combination therapy in part two.

2- Reduced Risk Of Severe Burn:

Narrow Band phototherapy cabinets solve the problems of over-exposure to ultraviolet by maximizing delivery of radiation (in the 311-312 nm range, the most beneficial component of natural sunlight) while minimizing exposure to superfluous UV. This allows patients to receive phototherapy treatments with less risk of severe burning or pathogenic exposure to UV in harmful ranges, because erythema of uninvolved skin is a limiting factor for UVB phototherapy [4].

3- More Therapeutic, Less Erythemogenic Activity:

Narrow-band, or TL-01, or 311 nm phototherapy has a higher ratio of therapeutic to erythemogenic activity, resulting in :

1-increased efficacy
2-reduced incidence of burning
3-longer remissions [4].

4- Results Are Similar To PUVA:

Remission periods are similar to those of PUVA therapy
and markedly superior to broadband UVB treatment[3].

5- Relatively Long Remission Period:

Studies showed 38-40 percent of narrow band treated patients required no more additional therapy for at least 12 months after discontinuation of therapy[4].

6- NB UVB Has An Antimicrobial Effect:

For the details of NB-UVB antimicrobial effect, see therapeutic trials, in part two .

7- NB UVB Increases The Effects Of Other Topical And Systemic Anti Psoriatic Therapies:

There are many reports showing the synergestic effect of NB UVB when used in combination with other topical and systemic therapies used in the treatment of psoriasis, NB UVB increases the effects of each of the following:

1-Calcipotriol
2-Anthralin
3-Psoralens
4-Retinoides.

For detailes see combination therapy in part two.

8- Contraindications Are Less Than Those Of PUVA:

NB UVB can be used in patients who have some PUVA contraindications such as abnormal liver function tests, abnormal kidney function tests,during pregnancy and lactation, and in patients below the age of 18 years, or even below the age of 12 years.

What are the disadvantages of NB UVB?

Lesional Blistering:

Four cases of unusual blistering occurred with narrow-band UVB phototherapy. Two asymptomatic and two painful episodes of blistering developed at the site of psoriatic lesions in the middle of a treatment course. These blisters were different from those that develop during PUVA therapy after minor trauma because they lacked erythema, resolved spontaneously, and occurred only on treated psoriatic plaques rather than on normal skin.

The significance, etiology, and frequency of such distinctive blisters remains unclear[23] .

Comments 1: We thought that this rare side effect should not be condsidered any more because it was reported only once in 1992 (almost 9 years ago). It could be due to inexperienced use of NB-UVB at that time or due to overdoses of NB-UVB, considering it not to cause any burning or blistering.

Surprisingly Calzavara-Pinton reported in the year 2000 that Asymptomatic blisters on psoriatic plaques are an uncommon adverse effect of TL-01 (UVB narrow-band 312 nm) phototherapy. He reported 7 new cases aiming to clarify the pathogenesis. Blisters were biopsied at different times after onset. Blood porphyrins and antibodies to nuclear antigens and the cell surface of keratinocytes were investigated. His study results showed 7 asymptomatic blistering eruptions strictly limited to recovering psoriatic plaques. Biopsies taken within 24 h showed junctional detachment and apoptotic necrosis of

basal keratinocytes. After 48 and 72 h, the blisters were intraepithelial, due to basal cell regeneration, and were no longer evident at 96 and 120 h. Dermal inflammation was always mild. Direct immunofluorescence tests as well as stainings for p53 protein did not show substantial changes. Blood investigations were negative. He concluded that TL-01 blisters are caused by the quick reduction of acanthosis and desquamation before defensive mechanisms, i.e. the increase in the thickness of the stratum corneum and pigmentation, develop. However, the pathogenetic mechanisms of apoptosis of keratinocytes remain unknown [24].

Comment 2 : Practically we could not see this blistering in our patients although we started almost 150 patients of several indications and some of these patients received a relatively high doses per session that may reach or exceed 5000 mj.

Complex Photodermatosis:

Patel reported an unusual case of localized solar urticaria which progressed on each occasion to polymorphic light eruption (PLE); this was initially noted following provocation by narrow band ultraviolet B (311-313 nm) phototherapy[21] . This also could be related to patient susceptibility or due to aggressive doses [25].

Carcinogenicity

Controversy:

Controversy exists as to the relative carcinogenicity of narrow-band versus broad-band UVB treatment. In 1988 Van Weelden and colleagues conducted a study with albino hairless mice that examined the tumor induction times for TL-12 broad-band bulbs compared to TL-01 narrow-band bulbs on the basis of equal acute responses.

The mice were irradiated every day, and the experiments were stopped when most of the tumors were larger than 4 mm. The results showed that narrow-band phototherapy had longer induction times for tumors smaller than 1 mm. In contrast, for larger tumors there was no difference in induction times between the two systems[26].

While in 1990 Van-Weelden stated that Phototherapy with narrow-band UV-B is an effective as PUVA in the treatments of psoriasis ; it is certainly more convenient and probably less carcinogenic[27].

Green-C also stated that narrow band at 311 +/- 2 nm (UVB) had the advantage of a reduction in burning and carcinogenic effects when compared with conventional broad band UVB therapy [28].

Later and in 1998 Hofer-A stated as well that near erythemogenic 311 nm UVB therapy may clear psoriasis faster than far erythemogenic therapy but that the latter regimen may be equally effective as it requires slightly more treatment sessions at a lower and possibly less carcinogenic cumulative UV dose [29].

Prediction Of The Phototumorigenic Potential Of Broad-Band (270-350 Nm) And Narrow-Band (311-313 Nm) Phototherapy:

The new Philips TL01 narrow-band (311-313 nm) and conventional broad-band (e.g., Philips TL12; 270-350 nm) sources are effective for psoriasis phototherapy, for which treatment regimens are based on a predetermined minimal erythema dose. TL01 phototherapy treatment times are approximately half those with TL12 for psoriasis, whereas the cumulative exposure doses at clearing are similar. Gibbs et al compared the phototumorigenic potential of TL01 and TL12 radiation in mouse skin. Groups of albino Skh-1 hairless mice were exposed for 5 d/week at three dose levels. At each dose level, TL12 and TL01 doses were equally edematogenic. At each dose level, TL01 radiation was significantly more effective at producing first tumors of 1 mm in diameter and multiple tumors. At the lower two dose levels, TL01 radiation produced a significantly greater proportion of squamous cell carcinomas. This study demonstrates that TL01 radiation is more phototumorigenic than TL12 radiation at equally edematogenically weighted doses. This is in contrast with previous reports that edema production by polychromatic sources is predictive of their phototumorigenic effect in Skh-1 mice. The absolute cumulative TL12 dose needed to induce tumors was much less than that for TL01 radiation.

The possibility of increased tumor risk with TL01 phototherapy should be considered but must be balanced against the high phototherapeutic efficacy of this source, short treatment times, and the low cumulative doses necessary for clearing of psoriasis[30] .

(End of part one. Part two starts with clinical trials. References will be continued from 32)

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