Review Article

Narrow band UVB phototherapy in dermatology

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HISTORICAL ASPECTS

The first report of the use of 'phototherapy' in the treatment of skin disorders dates from 1400 BC from India when patients with vitiligo were given certain plant extracts (whose active ingredients included psoralens) and then exposed to the sun.[1] The real interest in the use of ultraviolet (UV) irradiation in the treatment of various skin diseases started in the 19th century when Niels Finsen received the Nobel Prize (1903) for his therapeutic results with UV irradiation in lupus vulgaris, the only dermatologist ever to be awarded one.[2] This marked the start of modern phototherapy. It was used in thermal stations for the treatment of tuberculosis, in the treatment of leg ulcers in wartime, and various other skin diseases.[3] It was a very long journey from the use of plant extracts and sun exposure to treat vitiligo to the use of oral psoralens and total body UVA-irradiation cabins (PUVA) to treat various skin diseases. In a landmark development, in 1974 Parrish et al reported the useful role of high intensity UVA tubes in combination with oral psoralens in the treatment of psoriasis leading to what is now known as PUVA therapy.[4]

The history of UVB phototherapy is not as old as the history of photochemotherapy. Wiskemann introduced irradiation cabin with broad band UVB tubes in 1978 for the treatment of psoriasis and uremic pruritus.[5] However, broad band UVB phototherapy was less efficient for treating psoriasis than PUVA and so never achieved popularity. The breakthrough came after 1988 when narrow-band UVB (NB-UVB) phototherapy was introduced for the treatment of psoriasis by van Weelden et al and Green et al.[6,7]

THERAPEUTIC SPECTRUM

A potential advance in UVB-based phototherapy has been the introduction of fluorescent bulbs (Phillips model TL-01) that deliver UVB in the range of 310 to 315 nm, with a peak at 312 nm. It has a relatively narrow spectrum of emission which when compared with the older broad band UVB source has a reduction in erythemogenic wavelengths in the 290-305 nm range and 5-6 fold increased emission of the longer UVB wavelengths, thereby resulting in a higher phototherapy index for psoriasis.

MECHANISM OF ACTION

In the skin, NB-UVB radiation is absorbed by DNA and urocanic acid and alters antigen presenting cell activity. NB-UVB is about 5-10 fold less potent than broad band UVB for erythema induction, hyperplasia, edema, sunburn cell formation and Langerhans cell depletion

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from the skin. It has a relatively more suppressive effect than broad band UVB on systemic immune responses as judged by natural killer cell activity, lymphoproliferation and cytokine responses.[8] The mechanism of action of NB-UVB phototherapy has not been completely understood. In psoriatics, NB-UVB phototherapy lowers peripheral natural killer cell activity, lymphocyte proliferation and immune regulatory cytokine production by both Th1 (IL-2, IFN-γ) and Th2 (IL-10) T-cell populations.[8,9]

Similar to PUVA therapy, NB-UVB may exert its effects in vitiligo in a two-step process. Both steps may occur simultaneously, the first being the stabilization of the depigmenting process and the second, the stimulation of residual follicular melanocytes.[10,11] The well-documented immunomodulating effects of UV radiation can explain the stabilization of the local and systemic abnormal immune responses.[12] It is also likely that NB-UVB, similar to PUVA therapy, stimulates the dopa-negative, amelanotic melanocytes in the outer hair "root sheaths, which are activated to proliferate," produce melanin and migrate outward to adjacent depigmented skin resulting in perifollicular repigmentation.[11] The ability of NB-UVB radiation to systemically suppress the major components of cell mediated immune function is thus likely to be linked to its beneficial effect in several inflammatory skin diseases including psoriasis.

PHOTOTHERAPY UNIT

NB-UVB phototherapy cabins contain fluorescent TL-01 (100 W) tubes as the source of irradiation. The cost of a chamber and lamps show considerable variations between countries and distributors. NB-UVB cabins available commercially either incorporate TL-01 alone or in combination with UVA tubes. Combination chambers take longer to administer a treatment dose. Thus, although they provide flexibility, they may represent an unsatisfactory compromise for a busy phototherapy unit. Recently, shorter tubes of NB-UVB have also become available in small area treatment equipments (hand and foot unit, NB-UVB comb) for the therapy of localized body areas.

DOSING SCHEDULE

NB-UVB schedules can be tailored according to patient skin type and local experience. There are two regimens that are most commonly used; the first involves determination of the individual's minimum erythema dose (MED) by means of a separate bank of TL-01 tubes. Often 70% of the MED value is used for the first treatment; thereafter therapy is given three times or more in a week with 40, 20 or 10% increments depending on local experience and skin type tolerance. Another approach, as commonly practiced in India, involves a standard starting dose (280 mJ/cm^2), with stepwise increase (usually 20%) depending upon the patient's erythema response. In the photodermatoses, the approach is more cautious with only 10% incremental regimen on sun-exposed sites.[9] In case of mild erythema, the irradiation dose is held constant for subsequent treatments or until resolution of symptoms. The goal of therapy is to achieve persistent asymptomatic erythema. In case of painful erythema "with or without edema/blistering, further treatment is" withheld till the symptoms subside. After resolution of overdose symptoms, the dose administered is 50% of the last dose and subsequent increments should be by 10%.

INDICATIONS

1. Vitiligo

In India, vitiligo is associated with marked social stigma, thus demanding its effective management. NB-UVB is a new addition to the armamentarium of therapies for vitiligo. Clinical experience with NB-UVB in vitiligo is limited, with only a few published reports.[13,14,15,16] However, initial results have been encouraging and there is a growing interest in its use in vitiligo worldwide. While earlier reported studies have evaluated its role mostly in Western population, our experience in Indian patients is further evidence of its efficacy in the treatment of vitiligo.[17,18]

In 1997, Westerhof and Nieuweboers-Krobotova[13] first reported the use of NB-UVB phototherapy for the treatment of vitiligo. In their comparative study, 67%

of patients undergoing NB-UVB phototherapy showed repigmentation compared with 46% of patients receiving topical PUVA after 4 months of therapy. In a recently published study, NB-UVB was reported to be effective and safe in childhood vitiligo.[14] In this open trial, 51 children with generalized vitiligo were treated twice weekly with NB-UVB radiation therapy for a maximum period of 1 year, resulting in more than 75% overall repigmentation in 53% of patients and stabilization of disease in 80%.

Scherschun et al retrospectively analyzed their experience of treating vitiligo with NB-UVB administered as monotherapy 3 times a week.[15] Five of their seven patients achieved more than 75% repigmentation with a mean of 19 treatments, whereas the remaining two patients had 50% and 40% repigmentation after 46 and 48 treatments respectively. In a recent meta-analysis of non-surgical therapies in generalized vitiligo by Njoo et al,[19] higher success rates were observed with NB-UVB (63%) than with oral PUVA (51%). As in the western population, NB-UVB phototherapy produces a cosmetically good color match in Indian patients.[18] Its distinct advantages over PUVA include the lack of psoralen related side effects and precautions, cosmetically better color match, and its safety in children. However, the relative stability of NB-UVB induced repigmentation over PUVA, its maximum safe duration and cumulative dose allowed still remain to be determined.

2. Psoriasis

The NB-UVB lamp was developed as a 'new' UVB phototherapy source with an emission spectrum within the therapeutic waveband for psoriasis phototherapy. NB-UVB phototherapy has a higher ratio of therapeutic to erythemogenic activity, resulting in increased efficacy, reduced incidence of burning and longer remission. Results from two therapeutic action spectroscopy studies indicated that wavelengths of the range 295-320 nm are effective in clearing psoriasis, whereas shorter wavelengths are more erythemogenic, and wavelengths longer than 320 are less therapeutic.[20,21] Subsequent clinical studies have tended to report significantly greater improvement of psoriasis with NB-UVB including reduced incidence of burning episodes, increased efficacy and longer remission when compared with broad band sources.[22] When NB-UVB phototherapy and PUVA were compared, there was little overall difference in efficacy.[23,24] Coven et al compared the therapeutic effectiveness of half-body exposures to NB-UVB or broad band UVB in moderate to severe psoriasis.[25] Clinical resolution was achieved in 86% of sites treated with NB-UVB vs. 73% treated with broad band UVB including faster clearing and more complete disease resolution.

Although treatment with NB-UVB is reported to be highly effective in clearing psoriasis patients, whether this therapy represents a modest advance or a real breakthrough is not clear. If NB-UVB is to replace PUVA therapy in the treatment of more severe psoriasis, it must not only achieve a comparable clearance rate in psoriasis, but it must also maintain remission at a comparable frequency of treatment. At present, small studies do provide some hope in this respect.[26]

3. Atopic dermatitis

Fortunately atopic dermatitis (AD) is less severe in the Indian population and can be mostly managed by topical therapies.[27] Recently NB-UVB has been reported to be effective for the treatment of AD and is one of the first line therapies in moderate-to-severe AD in western countries.[28,29] To optimize the patient's personal comfort, air conditioning is incorporated into the irradiation cabin.[30] Available data indicate that NB-UVB seems to be a promising modality for the treatment of moderate-to-severe atopic dermatitis and is favorably accepted by patients. It offers an effective alternative to steroids for chronic severe AD.

4. Other dermatoses

Prophylactic low dose NB-UVB has been found to be useful in various predominantly UVA induced photosensitivity disorders like polymorphic light eruption, actinic prurigo, hydroa vacciniforme and the cutaneous porphyrias by providing a 'hardening photoprotective' effect. A typical course involves 10-15 treatments given in early spring.[31] We have also observed a beneficial role of NB-UVB in patients with airborne contact dermatitis to *Parthenium hysterophorus,* a frustrating problem for both the patient and the

Table 1: Narrow band UVB responsive dermatoses (*Dermatoses that may flare up)

Common indications
Vitiligo
Psoriasis
Atopic dermatitis
Other indications
Mycosis fungoides
Parapsoriasis
Generalized lichen planus
Pityriasis rosea
Pruritus
Seborrheic dermatitis
Pityriasis rubra pilaris
Prurigo nodularis
Scleroderma
Polymorphic light eruption*
Actinic prurigo*
Hydroa vacciniforme*
Porphyrias*

physician.[32] Other less frequently tried indications are listed in Table 1.

COMBINATION THERAPY

In psoriasis, NB-UVB has been used in combination with topical therapies like tar, dithranol, calcipotriol and tazarotene. There are some reports suggesting faster clearance, but the benefit of their combination with NB-UVB over NB-UVB used alone in the treatment of psoriasis is still debatable.[33,34] However, it should be remembered that for most patients an attractive feature of NB-UVB monotherapy is the absence of topical therapy. There is hardly any published information on the role of combination therapy in vitiligo. Broad band UVB has also been used in combination with psoralen (PUVB),[35] but its comparative efficacy and safety over NB-UVB and PUVA remain to be determined.

EVIDENCE BASED CURRENT USE

In Europe, NB-UVB phototherapy is being increasingly used for the treatment of various skin diseases including psoriasis. Irradiation with this source has been found to be superior to conventional broad band UVB in psoriasis, producing longer remissions, a lower incidence of burning and possibly a lower risk of UV carcinogenesis.[25,36] In an important attempt to develop evidence-based guidelines for the treatment of vitiligo, NB-UVB therapy was recommended as the most effective and safest therapy for generalized vitiligo.[37]

The general advantages of NB-UVB therapy over PUVA include safe use in children and pregnant women, no need for post-treatment eye protection, no drug induced nausea and no drug costs.

LONG TERM USE AND ADVERSE EFFECTS

As with other forms of UV exposure, in addition to the expected immediate sunburn effects, chronic NB-UVB exposure is likely to increase photoaging and the risk of carcinogenesis.[8] Presently there is insufficient human data available to provide recommendations regarding the safe maximum NB-UVB dose. However, according to a dose response model it has been calculated that the long-term risk for carcinogenesis with its use may be less than that of PUVA therapy.[38] Clinical experience with NB-UVB is limited and currently there is no established safe limit for its maximum safe duration of use in vitiligo. Njoo et al recommend that responsive patients can be given this treatment for a maximum of 24 months.[37] After the first course of one year, they recommend a resting period of three months to minimize the annual cumulative dose of UVB. In children, the maximum duration allowed is 12 months. Subsequently, if required, only limited areas should be exposed. If no response is observed after six months, further therapy should be discouraged. Further, the risk of cutaneous malignancies in vitiligo can be reduced by skin saving principles, i.e. covering the parts that have repigmented satisfactorily and shielding the genitals.

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