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Advances in phototherapy for psoriasis

Umashankar Nagaraju

Abstract:
Ultraviolet light has a wide spectrum of effects on human skin depending on the wavelength. Ultraviolet light often used for therapy of psoriasis comprises of electromagnetic spectrum ranging from 200nm – 400nm. Phototherapy of psoriasis is frequently used in combination regimens to achieve higher clearance rates, longer disease-free intervals, and to reduce the patient`s cumulative radiation dose thereby lowering the carcinogenic risk. Phototherapy may be combined with topical or systemic agents. Topical agents most commonly used are anthralin, tar, vitamin D analogues and tazarotene. Among systemic agents, retinoids are the most widely used. Ultraviolet B wavelengths in the range of 300-313nm is more efficacious than conventional broad-band UV-B [Philips TL 40W/12 lamp] and causes greater remission of psoriatic lesions. 311nm narrow-band UV-B (TL-01) phototherapy is more effective and probably has no greater risk than conventional UV-B (TL-12) phototherapy in the treatment of psoriasis.
Key words: Phototherapy, Psoriasis

Introduction:

Natural sunlight was used for treating various skin disorders, even before the advent of modern sciences. As the science advanced, phototherapy has developed to a greater extent providing hope for an easier, safer and more effective therapeutic modality.[1,2] Today phototherapy has greatly advanced with development in biotechnology having effect on specific steps in the pathogenesis of psoriasis, providing hope for an easier, safer and more effective therapy.[2,3]

Ultraviolet light often used for therapy of psoriasis comprises of electromagnetic spectrum ranging from 200nm – 400nm. It is divided into 3 bands : Ultraviolet C – 200nm to 290nm, Ultraviolet B –290nm to 320nm, Ultraviolet A – 320nm to 400nm.[4,5] UV-A administered in the presence of photosensitizers such as psoralen compounds (PUVA) serves as an excellent therapeutic tool.[5,6] UV-B radiation is responsible for the most beneficial effect of sunlight and conventional ultraviolet therapy. The latest development in the field of phototherapy is the introduction of 311nm- narrow band UV-B phototherapy which exploits the therapeutic action spectrum of psoriasis (300-313nm).[7,8] It is being effectively used not only in the treatment of psoriasis but also in atopic dermatitis, vitiligo and photodermatoses. Other new devices that have improved and expanded the spectrum of skin disease amenable to phototherapy are high-dose UVA-1 and photodynamic therapies. These new devices, along with newer combination therapies have led to a mini-revolution in phototherapy.[5,9]

Pathogenesis of psoriasis:

Pathogenesis of psoriasis is unknown. But many pathophysiologic abnormalities have been suggested and investigated. In psoriasis there is hyperproliferation of epidermis, with concomitant inflammation and vascular changes. Basal keratinocytes continue to express keratins K5/K14; however during keratinocyte differentiation, there is down regulation of cytokeratin K1 and K10 which are replaced by the hyper-proliferation associated keratins K6/K16.[10,11]

Psoriasis is characterized by preponderance of TH1 cytokines, namely interferon-ϒ, IL-2, IL-12, TNF-α with a

relative deficit of TH_2 cytokine profile, i.e converting towards a TH2 profile, reportedly causes clinical improvement of disease.[12,13] Interferon-ϒ present in high levels in the lesion and serum stimulates the keratinocyte expression of intercellular adhesion molecule-1 (ICAM) and HLA-DR.[13,14]

Phototherapy:

Ultraviolet light has a wide spectrum of effects on human skin depending on the wavelength. The effects of UV-B (290-320nm) on the skin are mediated by direct DNA chromophore damage caused by reactive oxygen species such as singlet oxygen.[15]

Photochemotherapy:

Photosensitizers like psoralens (8-methoxypsoralen) intercalate with DNA with the energy of ultraviolet rays. Psoralens covalently cross-link nucleic acids between opposing strands of duplex regions of DNA. The formation of these cross-linking bi-functional photoadducts leads to irreversible photo inhibition of DNA synthesis and mitosis.[2,10,16] This reaction is important in the hyper-proliferative psoriatic epidermis. In addition PUVA also suppresses the activation of lesional T-cells. The treatment regimen is divided into two phases:[2,7,17]

- The clearance phase with maximum frequency therapy and
- A maintenance phase after the clinical response.

Psoralen may be administered as 5-MOP, 8-MOP or trimethylpsoralen (TMP) as systemic, topical or as bath PUVA. This is followed by UVA (320-440nm) light exposure.

A maintenance phase after the clinic response extends benefit of the clearing phase treatment, while limiting the total exposure to UVL.

Phototherapy of psoriasis is frequently used in combination regimens to achieve higher clearance rates, longer disease-free intervals, and to reduce the patient`s cumulative radiation dose thereby lowering the carcinogenic risk.

Combination Therapy:

Phototherapy may be combined with topical or systemic agents. Topical agents most commonly used are anthralin, tar, vitamin D analogues and tazarotene. Others include glucocorticoids, emollients and salt water bath.[2,4,18,19] Among systemic agents, retinoids are the most widely used. Others include glucocorticoids, cyclosporine A, and methotrexate.[2,4,6]

Combination with Topical Agents:

Anthralin:

Antipsoriatic effect is due to its anti-inflammatory and immunosuppressive action. It inhibits keratinocyte proliferation in culture. The combination of phototherapy and anthralin for the treatment of psoriasis was first proposed by Ingram in 1953[20] and was modified later.[21] However anthralin is not favored by patients due to staining and dose depended skin irritation (anthralin erythema). Dithranol embedded in crystalline monoglycerides combined with phototherapy (UVB), offers a new approach in the treatment of psoriasis. It has been shown that this formulation combines adequate efficacy with low irritation and staining properties.[18,21, 22]

Coal Tar:

Crude coal tar (CCT) has a direct anti-proliferative effect preferentially affecting transformed kertinocytes in hyperproliferative psoriatic plaques and not those of the healthy skin.[23,24] Goeckerman regime for the treatment of psoriasis includes the use of crude coal tar. However, use of tar is not preferred because of poor patient compliance owing to its unpleasant odour and discoloration of skin and clothes. Application of tar can also lead to development of acneiform lesions, and in addition combination of tar with UV-B therapy has an increase carcinogenic risk.[18]

Vitamin-D analogues:
These include calcipotriol (also called as calcipotriene),calcitriol and tacalcitol. They have anti-proliferative, anti-inflammatory effects and enhances maturity of cells.[13] The main indications are psoriatic plaques of limited extent and lesions on the scalp, face, palms, and soles and in the intertriginous areas.[25,26] Calcipotriol plus UV-B twice per week has been found as effective as UV-B alone thrice per week, thus reducing patient visits. This also accounted for nearly 34% decrease in cumulative UV-B exposure, an important long-term benefit for patient receiving phototherapy for chronic plaque psoriasis.[27]

Salicylic acid:
It acts as keratolytic by removing scales and crusts and is used in the concentration of 2 to 10%. It is usually combined with coal tar, steroids and dithranol.[28]

Tacrolimus:
It is beneficial over sensitive areas like face where steroids may have troublesome side effects.[13]

Tazarotene:
Combining UV-B photo-therapy with tazarotene offer a valuable therapeutic option that is more efficacious and faster than UV-B phototherapy alone. Neither UV-A nor UV-B inactivates tazarotene, it lowers the threshold for erythema caused by UV-A and also the threshold for immediate pigment darkening caused by UV-B. Hence, when tazarotene is added, UV dose is decreased by one third.[29]

Salt-Water bath (Balneophototherapy):
Synchronous application of NB-UVB phototherapy and bathing in salt water solution irrespective of salinity is an effective treatment for psoriasis and is significantly better than UV-B expose alone.[30,31,32]The exact mechanism is unclear. The most important effect of salt-water baths prior to phototherapy include immuno-modulatory, anti-inflammatory and anti-proliferative effects due to high mineral content[33].

Topical Steroids:
The beneficial effects of combination of UV-B phototherapy with topical glucocorticoids are limited. Topical steroids are useful for treating psoriatic lesions in areas like scalp, groin, perianal area and umbilicus that are not easily accessed by UV irradiation and for treatment of lesions resistant to standard phototherapy.[34]

Emollients:
During phototherapy, application of emollients to the psoriatic plaques helps reduce the scattering of UVR caused by scales and allows the effective wavelength to penetrate into the viable tissue.[35] Application of a thin film of emollient enhances the efficacy of UV-B therapy whereas a thick film acts as a sunscreen.[36]

Combination with systemic therapy:

Retinoids:
Retinoids are the most widely used agent for systemic treatment in combination with phototherapy. They may be used in combination with UV-B or in conjunction with PUVA (RE-PUVA) therapy.[18,37] The use of retinoids is limited to pustular or erythrodermic psoriasis because of potential side effects.[38]

The advantages of this combination are:[2,18]

- Retinoids act synergistically with UV-B phototherapy exerting anti-psoriatic effects and hence reducing the cumulative UV-B radiation doses.
- They have anti-carcinogenic effects and hence lower the increase risk of skin cancer resulting from long term UV-B therapy.

Methotrexate:
The treatment involves 3 cycles of methotrexate initially, followed by the addition of PUVA on week days and methotrexate on weekend until clear, at which point PUVA alone is continued as maintenance therapy[18].

Cyclosporine :
Combination of PUVA with Cyclosporine gives good result in severe cases. Cyclosporine an immunosuppressive agent is given when intolerance to methotrexate

or acitretin or failure to other therapies occurs. It is of benefit as it clears psoriatic lesions quickly.[1]

311-Narrow band UV-B Phototherapy:

Ultraviolet B wavelengths in the range of 300-313nm is more efficacious than conventional broad-band UV-B [Philips TL 40W/12 lamp] and causes greater remission of psoriatic lesions. In the early 1980's, use of 311nm-NB-UVB (TL40/01 – a new fluorescent lamp) was introduced which proved superior in the treatment of psoriasis with a major emission peak at 311nm.[1,4] This exploits the therapeutic action spectrum for effective clearance of psoriasis. This new lamp appears to provide more effective and safer phototherapy for psoriasis than conventional UV-B given thrice weekly.[1,39,40]

In psoriatic patients, NB-UVB phototherapy leads to depletion of Langerhans cells, decreased leukocyte adhesion to the microvasculature, depletion of intra-epidermal T cells, and induction of IL-10 production from macrophages, which acts as an anti-inflammatory mediator.[4,41] The ability of NB-UVB radiation systemically to depress major components of cell mediated immune function is thus likely to be linked to its beneficial effects in psoriasis.

Advantages:

- The distinct advantages of NB-UVB over conventional broad-band UVB appears to be its faster and greater efficacy in patients whose disease is refractory to other modalities of treatment including standard UVB.[1,5]
- Longer periods of remissions.
- No specific irradiation devices are needed, as the Philips TL-01 fluorescent lamps can be fitted into conventional PUVA cabinets.[1,5]
- Though NB-UVB is as effective as psoralens – UVA (PUVA), the former is preferable in view of its less carcinogenic effect compared to PUVA, absence of psoralen induced nausea, absent drug cost, does not require post- treatment eye protection and can be used safely during pregnancy and childhood.[42]
- Very effective in guttate psoriasis and also in the lesions of plaque type.[1,40]
- Safe and effective for more widespread psoriatic lesions in HIV infection.[5,43]

UVB dose depends on the skin type determined by both the constituent color (inherent melanin content) as well as the facultative color (genetic capacity to tan). In our experience, the average Minimum Erythema Dose (MED) for narrow band UVB exposure for type IV skin is 600mJ (range 515-715mJ) and for type V skin 1100mJ (range 895-129mJ). Better therapeutic response can be obtained by starting the initial doses at 360-450 mJ for type IV skin and 600-825mJ for type V skin and gradually stepped up by 20% depending on the patients erythema response.[1,2,44]

Adverse Effects:

Early effects: [1,5,45]

- Inflammatory reaction including erythema, pain and warmth.
- Delayed tanning becoming visible in approximately 72 hours after exposure to UV-B and persists for weeks to months. It may also result in freckling especially in fair skinned individuals.
- Immunological suppression due to alteration of epidermal Langerhans cell morphology and function
- Even a single UV-B exposure can lead to approximate two-fold thickening of the epidermis and dermis which however settles back toward normal over a period of approximately 6 weeks.[45]

Late effects:[1,5,45]

- Photoageing occurs following long term and recurrent exposes leading to cumulative DNA damage.
- Photo-carcinogenesis: NB-UVB therapy is reported to be 2 to 3 times more carcinogenic than conventional broadband UV-B therapy. However,

the cumulative doses of NB-UVB to clear psoriasis are less than one third of those required by conventional UV-B.[42] Thus the long term cancer risk of TL-01 use is no more, and possibly less, than would be expected with broadband UV-B sources. In addition, current evidence, points to the conclusion that the chronic NB-UVB phototherapy associated skin cancer risk may be significantly less than that with PUVA.[42]

Phototherapy in psoriasis with HIV infection:

Phototherapy is considered in HIV infected patients when skin disease is responsive to UVR after assessing the risk benefit ratio wherein the anticipated improvement in morbidity following phototherapy justifies the potential risks. Phototherapy with UV-B, narrow –band UV-B (311nm), or PUVA is proved to be effective and safe in the treatment of psoriasis patients with HIV infection. No progression of the HIV infection due to phototherapy has been proven.[4,43,46]

Conclusion:

311nm narrow-band UV-B (TL-01) phototherapy is more effective and probably has no greater risk than conventional UV-B (TL-12) phototherapy in the treatment of psoriasis. Based on clinical trials comparing PUVA and narrow band UV-B, the latter should be considered the first line of treatment for psoriasis. In the near future it will not only replace broad band UV-B phototherapy, but may also significantly reduce PUVA use.

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Author details:

Corresponding author: Dr. Umashankar Nagaraju, M.D. Dermatology
Professor, Dept. of Dermatology, Venereology and Leprosy
RajaRajeswari Medical College and Hospital, Bengaluru- 560074

Email: usdermavision@gmail.com