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Review Article

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Phototherapy: A concise Review

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ABSTRACT

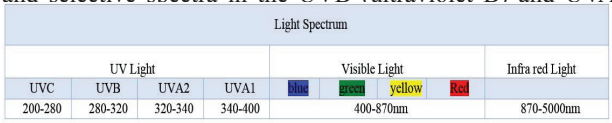
Phototherapy has been used in the treatment of varieties of skin diseases, different types of phototherapy are used in the treatment of those skin conditions; primarily for Psoriasis and Vitiligo for which phototherapy was first introduced, phototherapy compared with other systemic treatments has minimal side effects and limited contraindications.

In this review article the author will be highlighted on the importance of phototherapy in managing several photo responsive dermatoses, photobiology, types of phototherapy, the increasing indications for phototherapy and it`s side effects and contraindications .

Keywords- *Photobiology; Narrow band UVB; Systemic PUVA.*

INTRODUCTION

Phototherapy consists of exposure to ultraviolet radiation (UVR) for therapeutic reasons and it can be done using natural light, ultraviolet A (UVA) or ultraviolet B (UVB) light, to change cutaneous physiopathology in order to induce regression or control the evolution of dermatoses.[1] Already several thousands of years ago sunlight (heliotherapy) was used to treat a variety of skin conditions in Egypt, Greece and Rome.[2] Phototherapy using artificial light sources has a tradition dating back more than 75 years. Combination of topical crude coal tar and subsequent ultra violet (UV) irradiation for the treatment of psoriasis was introduced by Goeckerman in 1925 and became a standard therapy for psoriasis for half a century particularly in the United States. In the 1970 it was observed that broad band ultraviolet B radiation alone, if given in doses that produce a slight erythema, could clear the milder forms of psoriasis particularly seborrheic and gutate type. The introduction of PUVA (systemic Psoralens plus ultraviolet A) in the mid 1970s sparked a whole new series of discoveries, including high intensity UV sources and selective spectra in the UVB (ultraviolet B) and UVA



Photobiology: the wavelength region of Ultraviolet radiation extends from 100 nm to 400nm. It is divided into UVC (100-280), UVB (280-320) and UVA (320-400).[4-7] Wavelength between 200 and 280 of UVC is absorbed by the DNA, RNA and cell proteins as well as the stratum corneum and can be lethal to the viable cells of the epidermis. Because of its germicidal action, it is often called germicidal radiation.

UVB causes sunburn and is often referred to as sunburn spectrum. UVA is referred to as black light because it is not visible to the eye and causes certain substances to emit visible fluorescence [thus its use in Wood's Lamp].

The biological effects of UV radiation vary enormously with the wavelength. Photo biological response in the skin includes sunburn, pigmentation, aging and cancer.[3] UVR exerts different biological effects on different kinds of cells in the skin.[8] Both UVA and UVB lights are known to cause changes in the DNA of cells.[9] Owing to the filtering effect of the earth's atmosphere, almost all UVC radiation and approximately 90% of the UVB is absorbed, and UVA makes up approximately 95% of the UV radiation that reaches the earth.[10] UVA with its longer wavelength can penetrate deep Into the dermis (epidermis, papillary dermis and superficial vascular plexus), while UVB reaches only to the epidermis. It is mainly UVB that burns the skin because it possesses much more energy than UVA (energy is inversely proportional to wavelength).[10]

Types of phototherapy:

Phototherapy clinic	
Therapeutic modalities	Photo-test modalities
• Narrow band-UVB	• MED (minimal erythema dose) test
• Broad band-UVB	• MPD (minimal phototoxic dose) test
• Systemic PUVA (with psoralen tab)	• PLE (polymorphic light eruption) test
• Bath- PUVA (with psoralen solution)	• LE (lupus erythematosus) test
• Cream-PUVA (with psoralen cream)	• Photo patch test
• UVA1	• Photo provocation test (solar urticaria)
• KUVA (with khellin tab)	• Drug photosensitivity
• PUVB (with psoralen tab)	
• Photodynamic therapy	

Mechanism of action of photo(chemo) therapy:

Although it is not fully and clearly understood.[11] It can cause apoptosis of pathogenical T-cell [in psoriasis, mycosis fungoids and atopic dermatitis], mast-cell apoptosis[12] [in pruritic skin disorders] and apoptosis of keratinocytes.[13] While it causes enhancement of melanocyte proliferation [in vitiligo] and decreased release of histamine from both basophils and mast cells [in chronic idiopathic urticaria and urticaria pigmentosa]. Phototherapy has anti-

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inflammatory, anti-proliferative and immunosuppressant properties and its therapeutic success is likely due to a combination of these roles.[14] It causes inhibition of ICAM-1 up regulation by keratinocytes in inflammatory diseases (which acts as counter-receptor for lymphocyte function-associated antigen-1 on the surface of leukocytes), it may lead to down regulation of Th17 signaling pathway and decreased expression of IL-10 by keratinocytes, with a subsequent reduction of IFN-γ signaling and an anti-inflammatory effect.[15] Phototherapy has also been found to decrease the expression of IFN-γ-inducing cytokines IL-12, IL-18 and IL-23[15] while increases the expression of immunosuppressive cis-urocanic acid levels in the skin, resulting in suppression of cellular immune response and inhibition of antigen-presenting function of Langerhans cells.[16] In (PUVA) photochemotherapy, psoralens photoconjugate to DNA with subsequent suppression of DNA synthesis and cell proliferation. Reactive oxygen species production (derived from psoralens reacting with molecular oxygen) causes mitochondrial dysfunction and leads to apoptosis of Langerhans cells, keratinocytes and lymphocytes.[3] The therapeutic effect of UVA1 is related to the fact that its long wavelength penetrates the dermis more deeply than UVB. UVA1 radiation induces collagenase (matrix metalloproteinase-1) expression[2,17], T-cell apoptosis, and depletes Langerhans and mast cells in the dermis. UVA1 exposure stimulates endothelial cells to undergo neovascularization. [in atopic dermatitis, Morphea and Keloid].[18]

Indication for phototherapy:

Despite the introduction of numerous effective systemic medications and biologic agents in dermatology, phototherapy remains a reliable, and often preferred option for several dermatoses and the number of potential indications for such phototherapy is continuously growing[19], these indications may include: inflammatory skin conditions like: Psoriasis[2], Pityriasis rubra pilaris, Eczema (atopic)[20] (seborrhic)[21], Lichen planus[22], Pityriasis lichenoides (acute and chronic). Autoimmune diseases like: Vitiligo, Alopecia areata[23], Necrobiosis lipodica, Generalized grauloma annulare, Morphea[24,25], Scleroderma[26,27], Lichen sclerosis[28-31]and some Idiopathic photodermatoses: Polymorphic light eruption (PLE), Hydroa vacciniforme, Solar urticaria[32], Chronic actinic dermatitis.[33] The miscellaneous group may include: Mycosis fungoides (stages IA, IB, IIA)[34-37], Pruritus or Prurigo, Pityriasis rosea, Chronic idiopathic urticaria, Urticaria pigmentosum, Mastocytosis, Cutaneus graft versus host disease (GVHD)[38,39], Subcorneal pustular dermatoses[40,41], Purpura pigmentosa chronica, Lymphomatoid papulosa, Langerhan cell histiocytosis. Photo dynamic therapy (PDT) is effective in actinic keratoses on the face and scalp, Bowen's disease and superficial basal cell carcinomas (BCCs). Areas where photo dynamic therapy has potential beneficial effect include Viral warts, Acne, Psoriasis and Cutaneous T-cell lymphoma.[42]

***Adverse effects and contraindications for phototherapy*:**

Phototherapy is generally considered to be a low risk treatment option, particularly in adult populations.[10] Since its development, use of NB-UVB has been prompted by a combination of its therapeutic efficacy and good safety profile regarding acute adverse events. However, concerns with regard to long lasting consequences still remains unsolved[13], and due to its relative safety, UVB may be used in most populations, including children[43,44], pregnant and lactating women.[44,45] There is insufficient data available to provide recommendations regarding the safe maximum dose and duration of phototherapy in children[46], and it is limited by compliance issues. Choice of type of phototherapy and close monitoring, with parental partnership, is the key to successful treatment.[47] However, contraindications and side effects are known and should be considered before patients begin a phototherapeutic regimen. The adverse effects include: UVB may cause acute phototoxicity, with erythema and blistering[9], may also lead to tanning and if proper protective eyewear is not worn, UVB-induced keratitis.[9]

Systemic PUVA may also lead to erythema and tanning, photo-onycholysis, melanonychia and friction blisters of treated areas[10], If proper protective eyewear is not worn, PUVA-induced cataracts may also occur[9], acute side effects related to both UVA and UVB are: dryness and itching, folliculitits, provocation of herpes simplex and PLE.[16] Psoralens used for systemic PUVA may cause Nausea (30%) and Vomiting (10%) [8-methoxy psoralens more than 5-methoxy psoralens].[48] Chronic side effects include: dyspigmentation (hyper or hypo pigmentation), Tanning , Freckles and lentigines, Photoaging [Wrinkles, solar elastosis, dyspigmentation, telangectasia], possible development of premalignant lesions [Actinic keratosis, Bowens Disease].[16]

UVB and PUVA in HIV-infected patients:

Because most forms of medical treatment interfere with biological events in the course of accomplishing their beneficial task, unintended adverse effects are almost inevitable. Recent concern about the use of phototherapy in patients infected with the human immunodeficiency virus (HIV) illustrate this double-edged situation.[49] UVB has been shown to be effective and safe in HIV patients[50], although a small study did show activation of the virus in the skin.[51]The available data and theoretical considerations indicate that UVB is more likely to be a hazard than PUVA in an HIV-infected population. However it is presently impossible to advocate the use of PUVA in immunosuppressed individuals in general, but major hazards are unlikely.

***Photo carcinogenesis*:**

It is thought that PUVA is associated with a dose-dependent increased risk of non melanoma skin cancers but no increase has been documented with NB-UVB and long-term data are missing.[40,52,53] It is purported that NB-UVB therapy has a smaller risk of inducing skin cancer when compared with PUVA, even in patients requiring phototherapy for many years, although this has not been substantiated in long-term studies.[54,55] While increase in melanoma incidence following UV therapy is controversial[56], It is advisable to avoid acute over doses and high cumulative doses because both factors may predispose to potential carcinogenicity. Male genitalia should be shielded during every treatment session as they are particularly sensitive to the development of squamous

cell carcinomas (SCCs).

Contraindications to systemic PUVA[9,45]:

There aresome absolute contraindications like: Pregnancy and lactation, children aged less than five years, photosensitivity or photoexacerbated conditions (Albinism, Dermatomyositis, Lupus, Xeroderma pigmentosa), basal cell nevus syndrome, previous exposure to arsenic or ionizing radiation.

Relative contraindications include:

Children less than twelve years, cataract, immunosuppressed patients, severe cardiac, hepatic or renal diseases, history of skin cancers.

UVB has limited contraindications including[9,45]:

Photodermatoses, history of skin cancer or family history of melanoma and mentally impaired patients.

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