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Phototherapy-related ophthalmologic disorders☆

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Abstract Phototherapy is an effective treatment option for a variety of dermatologic disorders, and the list of indications for its use continues to grow with advances in technology and our understanding of disease processes. Commonly used types of phototherapy include PUVA, broadband UVB, narrowband UVB, photodynamic therapy, and intense pulsed light therapy. Each therapeutic modality can have adverse acute and chronic effects on periocular and ocular structures, including the conjunctiva, cornea, crystalline lens, and retina. There are many types of protective eyewear options available, including goggles and contact lenses that can be used to prevent damage to ocular structures during phototherapy, particularly if eyelid closure is incomplete.

Introduction

Phototherapy has been an important part of the treatment of dermatologic diseases for more than 3500 years, when ancient Egyptian and Indian healers used the combination of sunlight (heliotherapy) and ingestion of plant extracts for this purpose.[1] In 1903, Niels Finsen received the Nobel Prize for his use of phototherapy to treat cutaneous tuberculosis. Artificial light sources continued to be an important tool in dermatology, particularly with the development of Goeckerman therapy in the 1920s, which uses tar in combination with UVB to treat psoriasis.[2] In the mid-1970s, psoralen and UVA were used as a treatment for psoriasis, a procedure commonly known as PUVA photochemotherapy.[3] In the 1980s, Parrish and Jaenicke showed that monochromatic UVB therapy that eliminated wavelengths less than 296 nm was less erythemogenic and more effective than broadband sources.[4] Narrowband UVB (NB-UVB) phototherapy was subsequently developed and shown to be an effective treatment for psoriasis and a variety of other dermatoses.

In addition to the UV waveband, several other types of radiation are used to treat dermatologic diseases. Photodynamic

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therapy combines the use of topical or systemic photosensitizers and light sources that emit the excitation wavelength of the photosensitizer; the most common clinically used photosensitizer is the porphyrin precursor alpha-aminolevulinic acid (ALA). Intense pulsed light treatment uses a broad spectrum of radiation to target a variety of chromophores in the skin. Although phototherapy is an effective therapeutic option for several dermatologic conditions, treatment can result in both acute and chronic damage to ocular and cutaneous structures. Providers must, therefore, regularly monitor patients for unintended side effects and adjust treatment as needed.

UVB phototherapy

Broadband UVB radiation (280-320 nm), either alone or in combination with topical tar has been used to treat psoriasis for many years. In the 1980s, NB-UVB (311-312 nm) was found to be more effective than broadband UVB radiation, and it has now become the most widely used form of phototherapy.[4] UVB phototherapy is used to prevent polymorphous light eruption and to treat a large range of dermatoses including moderate to severe psoriasis, severe atopic dermatitis, vitiligo, pruritus, parapsoriasis, cutaneous T-cell lymphomas such as mycosis fungoides, pityriasis lichenoides, lymphomatoid papulosis, seborrheic dermatitis, and HIV-associated pruritic eruptions.

UVB radiation's effect on the skin is principally via absorption by chromophores, including DNA and urocanic acid, in the epidermis and dermis. These chromophores stimulate signal transduction pathways and cause decreased keratinocyte proliferation, depletion of Langerhans cells, induction of skin macrophages, immunosuppression, and T-cell apoptosis. This results in therapeutic suppression of the inflammation and lymphoproliferation that occurs in cutaneous disorders.

Short-term adverse effects of UVB phototherapy include erythema, xerosis, pruritus, blistering, and reactivation of herpes simplex. Long-term adverse effects include freckling, more advanced photoaging, and skin cancer. There is strong evidence that eyelid malignancies such as basal cell carcinoma and squamous cell carcinoma are associated with UV radiation.[5] A 2012 literature review of the carcinogenic risks of NB-UVB shows that no increased risk of skin cancer was detected in four studies, although the lack of prospective studies on patients treated with NB-UVB makes it difficult to truly assess its carcinogenic risks.[6]

Ocular photodamage from UVB radiation is also an important concern. Toxicity from UVB radiation is mainly due to the induction of cyclobutane pyrimidine dimers (CPD).[7] The anterior ocular structures provide a protective barrier from UVB-induced CPDs, and evidence of the association between ocular cancers, such as ocular melanoma and ocular surface squamous neoplasia, and UV radiation remain limited.[5,8] Nonetheless, UV radiation can cause deleterious effects to the eye and ultimately affect vision by damaging the cornea, conjunctiva, lens, and retina, resulting in several types of ocular toxicities (to be discussed in the following section). A recent study used manikin heads to quantitatively measure ocular exposure to solar UV radiation at different times throughout the day. This study showed that the time when the maximum UV irradiance occurred differed for direct versus ambient light.[9] This illustrates the importance of ocular photoprotection at all times of the day, with both direct and peripheral light, and in every season.[9]

Due to the known side effects of UV radiation on the eyes, it is common practice that patients must wear UV-blocking goggles for ocular protection during phototherapy. In situations where periocular lesions need to be treated, such as vitiligo, patients need to be instructed to close their eyes for the entire duration of UV exposure. Protective contact lenses may be worn to further protect against ocular damage, particularly when eyelid closure is incomplete.[10] Because NB-UVB is the most commonly used phototherapy, the effect of NB-UVB on the eye will be described in detail.

Ocular effects of narrowband UVB phototherapy

Although only a negligible amount of UV radiation is transmitted through the eyelid, damage to the cornea, crystalline lens, conjunctiva, and retina can occur if these structures are exposed during phototherapy.[11] Photodamage to the eye depends on wavelength, duration, intensity, and size of the radiation source as well as each structure's absorption potential and ability for self-repair (Figure 1).[12,13] The action spectrum for each structure of the eye represents the waveband of radiation that causes the greatest damage.[13] The action spectra for the conjunctiva, cornea, crystalline lens, and retina have been determined by performing studies in humans, rabbits, and rhesus monkeys (see later).[13–23] NB-UVB bulbs have a peak irradiance between 311 nm and 312 nm and produce low levels of radiation in the remaining UVB waveband. These wavelengths are within the action spectra for the cornea, conjunctiva, crystalline lens, and retina are therefore able to induce ocular damage.[13–15,21–23]

Cornea

The cornea is the transparent, dome-shaped window covering the front of the eye. It is a powerful refracting surface, providing two thirds of the eye's focusing power. The cornea absorbs the majority of UVB with only 3% to 8% of radiation being transmitted to deeper structures of the eye.[24,25] The action spectrum for the corneal damage occurs between 210 nm and 320 nm with the 270 nm wavelength being the most effective wavelength.[13,15] Without eye protection, an 11.98 mJ/cm^2 dose of radiation in the 250 nm and 320 nm waveband can begin to induce corneal damage during NB-UVB phototherapy.[10] Although the action spectrum for the cornea includes wavelengths below 250 nm, this waveband is assumed to contribute very little to