Ocular hazards of blue-light therapy in dermatology

Daniel P. Walker, BS,[a] Heidi R. Vollmer-Snarr, PhD,[b] and Cheryl Lee D. Eberting, MD[c]
Dallas, Texas; and Provo and Alpine, Utah

Blue-light phototherapy has become important in the treatment of many dermatologic conditions and as a result continue to be developed. Although blue-light therapy is successful, research shows that excessive ocular blue-light exposure may contribute to age-related macular degeneration and other vision problems. As blue-light therapy becomes increasingly more popular for clinical and at-home use, patients and operators of blue-light devices should be aware of its associated ocular hazards. Protective eyewear should be carefully selected and implemented with each therapy session to guard against the development of retinal disease. (J Am Acad Dermatol 2012;66:130-5.)

Key words: age-related macular degeneration; blue light; blue-light phototherapy; photodynamic therapy; phototherapy; retinopathy.

Blue-light phototherapy is used in the treatment of many skin conditions. Currently, blue light is widely used in the treatment of actinic keratoses,[1-4] basal cell carcinoma,[5-8] and acne.[9-12] Because of its distinct mechanism of action, relative convenience, cost-effectiveness, and overall efficacy, blue-light phototherapy continues to be studied for its use as a novel treatment for many other dermatologic disorders. Blue-light devices are not only used in the dermatology clinic, but are now available for over-the-counter use. Although blue-light phototherapy is widely accepted and thought to be harmless, research shows that excessive blue-light exposure may cause age-related macular degeneration (AMD)[13-17] and other ocular problems. Dermatologists and patients alike should be advised of the safe handling and ocular risks associated with these blue-light devices.

Abbreviations used:

ALA: aminolevulinic acid
AMD: age-related macular degeneration
PDT: photodynamic therapy
RPE: retinal pigmented epithelium

THE EFFECTS OF BLUE LIGHT ON THE RETINA

Research has long suggested that different wavelength ranges of light cause damage to the skin and eye. Ultraviolet light (180-400 nm) causes erythema and carcinogenesis, corneal photokeratitis, and lens cataracts.[18] Infrared radiation (2-50 μm) is primarily responsible for thermal hazards to the cornea and lens and contributes to their opacities. Blue light (400-480 nm), part of the visible spectrum, causes retinal damage (photoretinitis)[18,19] and is implicated in the pathogenesis of AMD, the leading cause of blindness in developed countries.

Studies have demonstrated blue-light damage to retinal photoreceptors directly through the photosensitive molecule, rhodopsin.[20] These blue-light-sensitive photoreceptors send vital information to nonvisual brain centers that mediate circadian rhythms, neuroendocrine and neurobehavioral responses, metabolic homeostasis, stress response, and production of serotonin and melatonin.[21-25] Irreversible damage to photoreceptive cells may disrupt these biological systems, resulting in associated problems including insomnia, memory loss, and depression.[26]

Moreover, several studies have shown that the retinal pigmented epithelium (RPE), a cellular layer attached to the retina and responsible for its nourishment, is damaged or destroyed by excessive blue-light exposure.[27-33] Research has implicated the accumulation of RPE lipofuscin, granules composed of proteins, lipids, and retinoids, to this damage.[34-36] The most documented retinoid component in lipofuscin that has demonstrated phototoxicity is A2E.[31,32,37,38] Photoirradiation of this bisretinoid generates singlet

From the University of Texas Southwestern Medical Center[a]; Department of Chemistry and Biochemistry, Brigham Young University, Provo[b]; and Alpine Dermatology.[c]
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Reprint requests: Cheryl Lee D. Eberting, MD, Alpine Dermatology PC, 144 S Main St, Suite 100, Alpine, UT 84004. E-mail: alpinedermatology@gmail.com.
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and triplet oxygen, thus forming harmful oxidized A2E derivatives that cause DNA damage[37,39,40] and apoptosis.[15,31,32,38-40] Research suggests that A2E slowly accumulates in the RPE over a lifetime and individual doses of blue light each contribute to the cumulative formation of cytotoxic photoproducts.[41,42] Individuals who are chronically exposed to blue light may be at higher risk of developing AMD.[13,14,16,36,41,43-50] A number of epidemiologic studies have found associations between increased light exposure over a lifetime and AMD.[14,16,41,49-53] However, there are inherent difficulties in accurately measuring cumulative ocular exposure to light over a number of years. Estimates are difficult to do retrospectively and some studies[54-57] have been less conclusive about the risks associated with chronic light exposure and development of AMD.

CAPSULE SUMMARY

- Blue-light phototherapy has become an important tool in treating many dermatologic conditions, and it is critical to understand its proper use and associated hazards.
- Even small amounts of blue-light irradiation can contribute to age-related macular degeneration and other ocular problems.
- The proper protective eyewear should be selected and used by both patient and operator during blue-light phototherapy sessions.

The amount of irreversible damage sustained by the retina depends on both the intensity and the duration of blue light transmitted.[40] Blue-light injury can result from viewing either an extremely bright light for a short period of time or from a low-dose exposure for an extended period of time.[18,32] Most manufacturers of blue-light devices follow guidelines for light exposure based on acute or subacute retinal phototoxicity. Although the loss of a minimal number of RPE cells associated with a single dose may not severely impair vision, the cumulative loss of these postmitotic cells may eventually lead to irreversible vision loss. Individuals with frequent exposure to moderate amounts of blue light from occupational devices should be aware that although acute threshold damage is often avoided because of manufacturer compliance with published safety guidelines, long-term damage, not immediately apparent, may appear over time.[58] Similar studies[59] have suggested that prolonged effects of blue light on the retina can result from intensities well below accepted safety levels. Thus, excessive blue-light exposure, regardless of intensity, should be avoided to prevent retinal disease.

BLUE-LIGHT PHOTOTHERAPY IN DERMATOLOGY

In recent years, blue-light phototherapy has become an essential tool for treating a growing number of skin conditions. The most common and clinically proven application for blue light is in photodynamic therapy (PDT). The mechanism of action of PDT mirrors a damage process observed in photoretinopathy.[11,60] Light activates biological or chemical photosensitizing agents in the skin or retinal tissues to form cytotoxic intermediates, including singlet oxygen. These cytotoxic species promote cell death in nearby target cells. Blue-light PDT is commonly used in combination with the topical photosensitizer aminolevulinic acid (ALA) or less commonly, with its counterpart methylaminolevulinic acid.

Blue-light PDT is frequently used in the treatment of actinic keratoses[1-4] and basal cell carcinoma.[5-8] Blue light alone or in combination with ALA also effectively treats acne by reducing the number of inflammatory and comedonal lesions—providing a safer alternative to retinoid drugs and their associated teratogenicities.[9-12] Other studies report the efficacy of blue-light PDT in the treatment of sebaceous hyperplasia,[61] warts,[62,63] and roseacea.[64,65] PDT is also used for improvement in overall cosmesis,[9,66] including decreased skin wrinkling,[67] improvement in hyperpigmentation,[9,67] and reduction of telangectasias.[9] This list is not exhaustive, and the number of skin conditions treated with blue light continues to expand as studies further explore the benefits of this relatively new technology.[11]

BLUE-LIGHT DEVICES

As the clinical use for blue light increases, so does the variety and availability of blue-light devices. The most commonly used light sources for blue-light PDT are the BLU-U (DUSA Pharmaceuticals, Wilmington, MA), ClearLight (Lumenis, Santa Clara, CA), and Omnilux Blue (Photo Therapeutics Inc, Carlsbad, CA) photosystems. These devices provide light near 417 nm, the maximum absorption peak for ALA therapeutics.[9,11] These systems are free-standing, stationary units that require the patient be brought close to the light source while a large area of skin is illuminated. BLU-U (DUSA Pharmaceuticals) and ClearLight (Lumenis) use narrowband fluorescent tubes that produce incoherent light, and Omnilux Blue (Photo Therapeutics Inc) uses a light-emitting diode array. Blue-light devices have also been developed for nondermatologic dental