FLASH

— 2023

NEWSLETTER

of the World Photodermatology Day,
Singapore, July, the 3rd 2023

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Summary

GIOVANNI LEONE MD

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Rome, Italy

Dear Friends and Colleagues,

Many of us had the chance to attend our World Photodermatology Day on July the 3rd at the WCD In Singapore.

This was the first time that we organized our World Photodermatology Day in collaboration with our US colleagues of the Photodermatology Society, and the collaboration of our two Societies has contributed to the success and to the high rate of attendance. This was the most important meeting in presence, dedicated to Photodermatology, to be organized after the Covid pandemic. For us it is the sign that we can start again and resume fully our activity. In the World Photodermatology Day 2023 we had the occasion to listen to the most representative speakers and experts in the field, coming from all over the world. The mutual collaboration of our two Societies in the establishment of a vast and exciting program has permitted to all the attendees to acquire knowledge on the different aspects of the practice of Photodermatology in different countries.

The aim of this special issue of "Flash", kindly supported by BIODERMA - NAOS **is to give an overview of the main topics that have been presented during the World Photodermatology Day**. We thank the speakers who have provided the abstracts of their presentations to be included in this magazine.

We want to dedicate this special issue of "Flash" to two of our mentors, senior colleagues and renowned authorities in the field of Photodermatology who passed away in the last 6 months: Prof. John L.M. Hawk from London, who has been one of the founders of the European Society for Photodermatology and Prof. Herbert Hönigsmann, one of our honorary Board Members, and great expert in the field of Photodermatology.

I take also the occasion to thank, Elizabeth Buzney, President, Anna Chien, and Sewon Kang, Board Members of the US Photodermatology Society, who have been closely working with us to prepare the program of the World Photodermatology Day 2023 and have contributed to the success of the event.

You will find in this special issue of "Flash" also the contributions of the awardees of the Photodermatology Prizes offered by BIODERMA: one best oral presentation and two best posters in Photodermatology.

Thanks to all our presenters for their contribution and constant commitment in this area. I hope that you will appreciate the inputs coming from all over the World. Enjoy!

Singapore, July 2023

PROFESSOR JOHN HAWK

Former President of the European Society for Photodermatology (ESPD), sadly passed away on Christmas Day last year.

John Lyndon McLeod Hawk was born in the city of Hamilton, New Zealand, in 1942. He won a scholarship as the top pupil in languages in his final school year in his hometown. However, he decided to study physics at Auckland. He received his medical degree from the University of Otago, Dunedin, in 1969. After he moved to London in the early 1970s, he trained in dermatology at St Mary's Hospital and Guy's Hospital before securing a consultant post at St John's Institute of Dermatology. He succeeded Professor Ian Magnus as the Head of the Department of Photobiology (now Photodermatology) at St John's, a position that he held for thirty years, until his retirement in 2006.

Professor Hawk helped to establish the British Photodermatology Group in 1988 of which he was the chairman between 1991 and 1993. He was the president of the St John's Dermatological Society in 1997/98. He served for many years as British Association of Dermatologists' press liaison officer.

Professor Hawk was internationally renowned and was one of the founders and former president of the ESPD. He was also a founding committee member of the American Photomedicine Society. He was a president of the scientific committee of the European Academy of Dermatology and Venereology (EADV) and a member of the European Dermatology Forum. He was the deputy president and scientific committee chairman of the EADV Congress in London in 2005 and the president of the World Congress on Cancers of the Skin in Edinburgh in 2014.

In 1979, Professor Hawk and Professor Magnus coined the now widely accepted term chronic actinic dermatitis to encompass four diagnoses, namely persistent light reactivity, actinic reticuloid, photosensitive eczema and photosensitivity dermatitis. He promoted the benefits of lifetime photoprotection through his talks at the meetings and media appearances, whilst also recognizing the sun's importance to well-being. He initiated a lot of clinical research and published multiple scientific papers on photobiology and phototherapy. He has written chapters in all major dermatology textbooks as well as several books. He was a former editor of the journal Clinical and Experimental Dermatology.

Professor Hawk enjoyed many other interests. He was excellent in playing rugby and cricket during his university days. He was passionate about the All Blacks, New Zealand's national rugby team. In his retirement he continued to pursue his love for foreign languages and studied French. He travelled to around one hundred countries and was a great ambassador of photobiology.

Professor Hawk was charming, charismatic, enthusiastic and open-minded. He was loved by his patients and staff who enjoyed working with him. Many members of the ESPD have known Professor Hawk for many years, as a colleague, teacher and friend, and will be saddened with his passing.

Professor Hawk is survived by his wife Lorna, paediatrician, their two sons Simon and Tim, and five grandchildren.

Dr. Ljubomir Novaković
London

PROFESSOR DR. HERBERT HÖNIGSMANN

The entire community of photodermatologists and photobiologists mourns the untimely death of teacher and friend Prof. Dr. Herbert Hönigsmann, who passed away on 21.8.2023 in Vienna.

Herbert Hönigsmann was born on 26.3.1946 in Vienna. He studied human medicine at the University of Vienna (1962-1968) and was resident in the Department of Dermatology I from 1969-73. In 1976 he followed Klaus Wolff as senior physician at the Department for Dermatology in Innsbruck, where he established an outpatient clinic for radiation and phototherapy. Herbert Hönigsmann returned to the Department of Dermatology I in Vienna in 1981, and assumed the position of managing senior physician of the department. With the move from the old to the new University Hospital in Vienna, he was appointed Head of the Department of Special Dermatology and Environmental Dermatoses (1992-2008) and was Head of the Organizational Unit of the Department of Dermatology from 2004-2008. Herbert Hönigsmann retired in October 2008 but continued to care for his numerous patients.

Herbert was an innovator, a scientist and a great clinician. His name is closely linked to the fields of photobiology and photodermatology, of which he was a profound connoisseur of all aspects at 360 degrees. Together with Klaus Wolff and the Harvard Group around Thomas B. Fitzpatrick and John A. Parrish, he participated in the first studies on PUVA therapy, both with oral and topical administration (so-called bath-PUVA) for inflammatory dermatoses, such as psoriasis, vitiligo and atopic dermatitis, as well as cutaneous lymphomas in the 1970s. His name is also linked to the combination of PUVA with oral retinoids known as Re-PUVA, which increased efficacy and reduced the risk of long-term adverse events. From the 80s he participated in the development of basic knowledge and clinical applications of narrowband UVB and UVA1 phototherapies and from the 90s in the development and advancement of photodynamic therapy. In recent years, he has followed the positioning of phototherapy as a still valid therapeutic tool in a dermatological world, where new immunotherapies have been increasingly establishing themselves. We also must not forget his relevant contributions in the study of photoprotection and of the pathogenesis and therapy of photodermatoses.

Herbert Hönigsmann was a reference figure in the European and international scientific and photobiologic communities. He participated as a leader in numerous scientific societies knowing how to bring a fundamental impulse to scientific research. He also had the rare ability to bring harmony and serenity even in the most complex situations.

He was the generous mentor and stimulus to a generation of young researchers, but above all he was a true friend to many, and this is how we will remember him.

Prof. Piergiacomo Calzavara-Pinton
Dr. Bernhard Ortel

The effects of light in skin of color

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Solar radiation reaching the surface of the earth is divided primarily into ultraviolet radiation (UV, 290-400 nm), visible light (VL, 400-760 nm), and infrared (IR, 760 nm-1 mm). Each portion has distinct effects on the skin and these effects differ across skin types. This variation stems from the unique skin biology across these groups.

With UV exposure in skin of color (SOC), well-recognized characteristics include decreased sensitivity to the erythema caused by UV and greater melanin increase following irradiation. UV also causes reactive oxygen species formation and with the greater eumelanin content in SOC, these individuals are better guarded against the pro-oxidative effects of UV light. In SOC, there is also more protection against UV-induced DNA damage given the distribution of melanin within the upper epidermis, which protects the lower epidermis, home to keratinocyte stem cells and melanocytes. This epidermal melanin also protects these individuals against dermal matrix breakdown thus explaining their delayed onset of photoaging.

More data is emerging regarding the effects of visible light on the skin. VL can induce erythema, generate free radicals, and increase the production of inflammatory cytokines as well as matrix metalloproteinases. Data shows that these effects can occur even with low-level VL exposure. Similar to UV, the differential responses to visible light in light and dark skin are highly pronounced. Perhaps the most striking feature is the more intense and sustained pigmentation seen solely in SOC following VL irradiation. There is evidence demonstrating that while melanin may be protective against UV exposure, it may be a mediator in VL-induced phototoxicity.

Infrared can also have appreciable effects on the skin such as erythema and pigmentation although the data is more limited. The chronicity of IR exposure can also differentiate therapeutic from detrimental effects. A single dose of IR irradiation can lead to increased expression of transforming growth factor-βs (TGF-βs) in human skin and an upregulation of pro-collagen I. However, repeated exposure results in increased matrix metalloproteinases-1 expression, with a reduction in TGF-βs and procollagen I. Similar to UV and VL, IR can also have differential effects in light and dark skin types with individuals having more personal pigment being more protected against infrared radiation.

Cutaneous effects of the electromagnetic spectrum encompass wavelengths in ultraviolet, visible light, and infrared ranges. Individuals of skin of color have unique skin properties that result in differential responses to solar irradiation. This results in distinct features of photoaging seen in this population. More research is needed to understand the effects of light in SOC to develop improved photoprotective modalities and photoaging treatment strategies.

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Keratinocyte carcinoma chemoprevention with pharmaceuticals and dietary constituents

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Most keratinocyte carcinomas are caused by excessive exposure to ultraviolet radiation.

Methods for their prevention have focused on sun and tanning bed avoidance and treatment of actinic keratoses, which are keratinocyte carcinoma precursors. Despite these measures, keratinocyte carcinomas remain a global health problem.

Because molecular and biochemical alterations accrue in epidermal cells over long intervals, there is ample opportunity to intervene to inhibit, reverse and/or delay their occurrence.

There has been substantial progress in preventing the onset of keratinocyte carcinomas with niacinamide, retinoids, vitamin D and eflornithine. Promising dietary interventions include a low-fat diet, pomegranate, and grape extracts. Our studies have shown that cyclooxygenase inhibitors are very effective and that table grapes have potent anti-cancer activities.

Oral photoprotection for light and dark skin phototypes

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The solar spectrum is composed of various wavelengths: while longer wavelengths penetrate deeper into the skin, shorter ones may have both different and overlapping effects.

In this regard, ultraviolet (UV) radiation (UVR) constitutes 2-5% of solar radiation at the terrestrial level and is made up of UVA and UVB leading to DNA damage and production of reactive oxygen species (ROS) promoting harmful biological and clinical effects. In addition to UVR, there are other solar spectrum regions such as Visible Light and infrared radiation that represent 41% and 50% respectively, which are able to induce pigmentation and aging. Fitzpatrick skin phototype ranges from I to VI are perhaps the single most relevant factor in determining skin response to solar radiation in the form of sunburn and tanning during unprotected sun exposure, both mediated by DNA damage. Pharmacological photoprotective measures can be topical or oral. Novel and classic oral agents (e.g., vitamins, minerals, polyphenols, carotenoids) are safe and endowed with photoprotective and anti-photocarcinogenic properties. These compounds may increase systemic protection against the damaging effects of electromagnetic radiation in the UV, visible, and infrared ranges. Photoprotective mechanisms based primarily on antioxidant activities include anti-inflammatory, anti-pigmentary and immunomodulatory effects.

Considering this scenario, a relatively recent trend in skin care is the use of oral supplements that provide systemic photoprotection. Most of these usually do not avoid real erythema but can effectively prevent DNA damage, Langerhans cell depletion, pigmentation, photoaging and photocarcinogenesis. The mechanisms are poorly described, although a hypothesis is the increase in the basal level of antioxidant activity and replenishment of natural skin antioxidant systems.

There is increasing evidence regarding state-of-the-art systemic photoprotection using vitamins, vitamin derivatives and botanical and non-botanical dietary agents in humans. It has demonstrated beneficial effects by providing additional protection in specific population subsets.

The state-of-the-art approaches regarding the systemic photoprotective capabilities shown in humans of vitamins and vitamin derivatives, dietary botanical, and non-botanical agents and data supporting their beneficial effects as a measure of additional measure in specific subsets

of populations including those individuals prone to skin cancer (light skin phototype) or susceptible to pigmentary disorders (dark skin phototype).

Discussion will focus on the most scientifically supported oral photoprotectants: Vitamin D, Nicotinamide, and the Aqueous extract from the leaves of the fern Polypodium leucotomos registered and known as Fernblock®.

a) Vitamin D

25(OH)D3 exerts its functions through two signaling pathways. The genomic effects take place via the vitamin D receptor (VDR) that is considered a tumor suppressor. This receptor is expressed by various human cell types and modulates cell growth, differentiation, and apoptosis processes. It has been shown that vitamin D3 regulates pro-inflammatory mediators through the induction of arginase-1 expression (an anti-inflammatory enzyme), reducing the releasing of TNF-α, NF-κβ, NOS and decreasing COX-2 expression. All this leads to attenuation of inflammatory response. Administration of vitamin D3 seems to be a useful strategy against photocarcinogenesis. This compound mitigates the harmful effects of UVR, reducing sunburn and skin photodamage.

b) Nicotinamide

Nicotinamide is the active form of vitamin B3. Nicotinamide is a precursor of essential coenzymes such as nicotinamide adenine dinucleotide (NAD+) which is a substrate of PARP-1, an enzyme that detects DNA damage and promotes effective repair. It is also a cofactor for adenosine triphosphate (ATP), which plays a key role in DNA repair. Nicotinamide can prevent UVR-induced ATP depletion and subsequently replenish cellular energy which also enhance DNA repair and reduce photoimmunosuppression. Several clinical trials in immunocompetent subjects have shown effectiveness of nicotinamide treatment by reducing the incidence of nonmelanoma skin cancer and preventing its development. Regarding melanoma, systematic review and meta-analysis of randomized controlled trials showed no difference in risk of melanoma after nicotinamide treatment. Very recently, a double-blind clinical trial on organ-transplanted patients found no effect vs. placebo.

c) Polypodium leucotomos extract (Fernblock®)

Oral administration of single doses of this extract shows not only an antioxidant effect and inhibition of lipid peroxidation of skin cell membranes, but also reduces skin inflammation that occurs after exposure to UV radiation, prevents isomerization of trans-urocanic acid to its cis-4 form and protects against photoimmunosuppression. A particularly important effect of this Polypodium leucotomos extract after oral administration is the reduction of UV-induced Langerhans cell depletion and the induction and activation of the p53 gene with a direct role in accelerating the removal of DNA photoproducts, mainly highly mutagenic thymine dimers. In this context, the extract of Polypodium leucotomos has also been shown to prevent oxidative DNA damage, inhibiting the conversion of guanosine to 8-deoxyguanosine and reducing mutagenesis induced by UV radiation. All of this plays a significant role when administered to light skin phototype individuals. In this sense, a multi-center prospective, randomized, assessor-blinded trial lasting one year demonstrated that specific topical and topical + oral treatment with Fernblock® in subjects previously treated for AK and field cancerization (therefore at risk of recurrence), improved AK manifestations and prevented development of new lesions. On the other hand, recent work has demonstrated that oral administration of this extract also prevented UV-induced hyperpigmentation in dark skin phototype individuals by reducing melanin photooxidation and Vis-induced expression of opsin 3.

Photodynamic therapy in Singapore. Choosing the right treatment for the right patient

Eugene TAN

Photodynamic therapy (PDT) is a valuable tool in the armamentarium of non-surgical treatments for actinic keratosis and non-melanoma skin cancers. It involves the therapeutic use of a photochemical reaction generated from the interaction of a photosensitizing agent, visible light and oxygen to selectively destroy targeted diseased tissue. PDT can be employed as lesion-directed or field-directed therapy.

The photosensitizers and their corresponding light source used for illumination in PDT vary across countries.

In Singapore, methyl aminolaevulinate (MAL) 16% cream is used as the photosensitizer for PDT. Conventional PDT utilizes a red lamp (630-635 nm) for illumination, while daylight PDT leverages on the use of natural sunlight which is abundant all year round in this region.

Locally, the approved indications for conventional MAL-PDT include actinic keratosis, Bowen's disease as well as superficial and nodular subtypes of basal cell carcinoma. Conventional PDT is particularly useful in cases where surgery is practically challenging, such as large lesions or lesions at cosmetically sensitive sites such as the nose, ears and face. It is an effective treatment option for thick hyperkeratotic actinic keratosis, as well as Bowenoid actinic keratosis.

Daylight PDT is indicated for the treatment of actinic keratoses that are of mild-to-moderate thickness (Olsen Grade I to II). Being relatively painless, it is also useful as a field-directed therapy for large areas of field cancerization. In patients with multiple actinic keratoses on a background of photodamaged skin on the scalp, face and/or extensor forearms, daylight PDT will be an ideal treatment modality.

Apart from its predictable reaction and high therapeutic efficacy, the main advantage of PDT lies in superior cosmesis compared to other treatments such as cryotherapy, topical 5-fluorouracil and surgery. PDT is known to have suppressive effects on fibroblasts, which reduces the risk of developing hypertrophic or keloidal scarring post-treatment.

In Asian patients with darker skin types, post-inflammatory hypopigmentation after PDT is common though this improves over time. Disadvantages of PDT include pain and high treatment cost. For the vast majority of patients, pain during red light illumination in conventional PDT is tolerable and can be mitigated with distraction, cold water spray, as well as oral and/or local anaesthesia.

Given the availability of other treatment modalities, the decision to use PDT should be individualized and made after a thorough discussion with the patient, weighing the clinical need and benefits versus the risks and cost of the treatment. It is important to understand the advantages and disadvantages of conventional PDT and daylight PDT, so that the appropriate PDT modality can be deployed.

A case-based approach will be used to illustrate the various clinical scenarios whereby PDT may be considered for the treatment of actinic keratoses and non-melanoma skin cancers.

Significance of photon density on UV radiation: Implications on phototherapy

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Human beings have intricate relationship with the different spectrums of sun exposure. Among different solar radiation spectrum, the ultraviolet (UV) radiation has long been recognized to have significant impact on human health.

Clinically, UV radiation is frequently used to treat different dermatologic conditions. More specifically, UV phototherapy is known for its immune suppressive and bio-stimulatory effects. It has long been recognized that wavelengths and fluence (mJ/cm^2) play a significant role determining the biological effects of UV radiation on the skin. However, the effects of photon density (mW/cm^2; irradiance) on UV radiation have been less studied. Recent works have shown that photon density is an important factor determining the regenerative, immune modulatory, and carcinogenic effects associated with UV radiation. Clinical reports demonstrated that UVB radiation at higher irradiance induces more efficient repigmentation in the vitiligo skin. Higher activation of aryl hydrocarbon receptor signaling induced by higher irradiance UVB radiation as compared to its lower irradiance counterpart at equivalent fluence contributed to this observed phenomenon. Additionally, at equivalent fluence, UVB radiation at higher irradiance were reported to be more efficacious at immune suppression as compared to its low irradiance counterpart. Modulation of dendritic cell surface markers via aryl hydrocarbon signaling contribute to this observed phenomenon. Finally, photo adaptation plays a significant role determining the efficacy of phototherapy. It is revealed that at equivalent fluence, low irradiance UVB induces significantly more epidermal thickening as compared to its high irradiance counterpart. Therefore, when using UVB emitting devices at different irradiance, the difference in photo adaptation resulting from different irradiance should be considered when designing the treatment protocol. Understanding the impacts and mechanisms involved with UV radiation on the skin in terms of different photon density will allow us to provide phototherapy for our patients with better treatment results.

In vivo effect of far-UVC

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Ultraviolet radiation C(UVC) is widely used as an artificial light source, such as 254nm-UVC germicidal lamps. We reported the effects of recently developed far-UVC germicidal lamps that can be used safely in vivo. In this report, we defined the far-UVC as 200-230nm.

We introduced the study of far-UVC germicidal lamps, including our research from three perspectives:

1. Germicidal effect
2. Effects on skin and eyes
3. Investigation of the safe wavelength range

Germicidal effect

Similar to 254 nm-UVC, it is reported that the DNA of bacteria and viruses forms pyrimidine dimers by irradiation with the far-UVC, making lethal changes, and suppressing their growth, thereby sterilizing them. The far-UVC has a higher absorption rate for proteins than 254 nm-UVC, but the germicidal mechanism specific to the far-UVC is not fully elucidated yet.

Previous studies comparing 193 nm and 254 nm UV on the formation of pyrimidine dimer-specific endonuclease-sensitive sites assay and the colony-forming ability using several cell strains indicated that the outcome ratio between the two wavelengths was significantly different between the two assays. Therefore, it was suggested that UV-induced cell death by 193 nm involves factors other than pyrimidine dimer formation. On the other hand, the ratio of D37 (the dose which gives 37% survival) of the two UV sources indicated that the ratio of D37 by 193 nm UV irradiation to D37 by 254 nm UV was much more higher in XP cells than NHF, indicating that pyrimidine dimers are formed also by 193 nm UVC at least to a certain extent. Studies with irradiation of the far-UVC have shown that it has a germicidal ability against a wide range of microorganisms and is particularly effective in sterilizing bacterial endospores.[1] Furthermore, in the study of SARS-CoV-2 with irradiation at 0.1 mW/cm^2 for 30 seconds, they evaluated the reduction of SARS-CoV-2 by 99.7% in vitro as assessed using the TCID50 assay.[2] In addition, SARS-CoV-2 was entirely inactivated specimen samples from SARS-CoV-2 patients by irradiation of 81 mJ/cm^2 using the far-UVC lamp.[3]

Effects of skin

First, we evaluated CPDs formation in the epidermis of hairless albino Xpa(xeroderma pigmentosum group A) gene knockout mice (hereafter Xpa-knockout), which are hypersensitive to UV, and hairless albino wild-type (hereafter wild-type) mice. Very faint staining for CPDs was recognized in the uppermost part of the epidermis, the subcorneal region, but not for the basal layer after irradiation with the far-UVC at a dose of 5.0 kJ m^2 in both genotypes of mice.[4] Next, we investigated skin carcinogenesis in mice irradiated with the far-UVC lamp along a protocol that almost Xpa-knockout mice would develop skin tumors after ten weeks of irradiation with broad-band UVB followed by 15 weeks of observation. We observed no tumors in any of the mice with 222-nm UVC irradiation.[4]

Finally, we evaluated the backs of 20 healthy subjects irradiated with 500 mJ/cm^2 by the far-UVC lamp. No erythema was observed on the back 24 hours after irradiation. We checked the amount of CPD produced by the far-UVC in the skin 1 hour after irradiation by ELISA. The amount of CPD in the irradiated region was more significant than that of the non-irradiated area and negative control. We considered that this result was due to the evaluation of CPD formed in the superficial layer of the epidermis.[5]

Eyes evaluation

We introduced the results of acute reactions in rat eyes irradiated with the far-UVC. In the group irradiated with 254 nm UV, erosion was observed in corneas exposed to 600 mJ/cm^2, but in corneas irradiated with the same dose with the far-UVC, no damage and no CPD-positive cells were observed.[6]

Next, the eyes of mice that were irradiated for chronic evaluation of skin were evaluated in the same way as skin. Compared to the group irradiated with broad-band UVB, in which we observed ulcers in the corneal epithelium, corneal opacification, cataracts, and retinal degeneration, we observed no significant changes in the group irradiated with the far-UVC, regardless of genotype.[4]

Long-term effects on the human eyes were reported by Sugihara *et al*. When six ophthalmologists' eyes and lids were irradiated within threshold limits by the far-UVC, they observed no acute or chronic adverse events for 12 months prospectively.[7]

In addition, although there is no chronic evaluation study of irradiation with the far-UVC skin in dermatology, they reported that no erythema was observed on the eyelid skin in this study.

Investigation of the safe wavelength range

Unlike the far-UVC lamp, it has been reported that pyrimidine dimers were formed up to the basal layer in the study irradiated with a krypton chloride excimer lamp without a filter cut-off wavelength above 230 nm. We examined the range of wavelengths that are harmful *in vivo*. We tested the *in vivo* effect using the improved device in which the integrated intensity of 235-280 nm was reduced to less than 1% of irradiator before improvement.[8]

When we irradiated 100 kJ/m2 with the improved irradiator, we observed a significant reduction of CPDs-positive cells in the epidermis. Next, we defined any subtle cutaneous response after irradiation as the minimum perceptual response dose (MPRD) of 222 nm, 235 nm, and 254 nm based on predetermined conditions to evaluate similar effects of the skin irradiated with each lamp.

CPD-positive cells were only observed in the top layer of the epidermis irradiated with 1 MPRD at 222 nm-UVC. When 235 nm UV-C was irradiated with 1 MPRD, CPD-positive cells were observed up to the basal layer. Similar results were obtained in a study of penetration depth of the far-UVC in the limbic cornea of rats.

Finally, based on the fact that the action spectra of erythema induction are well correlated with thymidine dimer formation in the upper epidermis between 280 and 340 nm, we overlaid our curve of MPRD data over an estimated MED spectrum multiplied by two factors, that is, the reciprocal of the action spectrum of the induction of thymine dimers (CPDs) to the reciprocal of the transmittance value of both mouse and human through the stratum corneum.

As a result, the MPRD was consistent with the estimated MED spectra and had higher thresholds than the spectra from previous animal experiments and TVLs for acute reactions by UV exposure.

In the present study, we observed a 10-fold difference in 1 MPRD between 222 nm and 235 nm UV.

The study by irradiation with UVB has reported that the effect *in vivo* between 300 and 320 nm region has drastically changed.[9]

The results of our study suggested that even in the 230-235 nm region, the effects *in vivo* may change significantly.

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[4] N. Yamano *et al.* Photochem Photobiol. 2020 Jul;96(4) PMID3222977
[5] T. Fukui *et al.* PLoS One. 2020 Aug 12;15(8) PMID32785216
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Epigenetic regulation of skin aging

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UV radiation accelerates skin aging through complex epigenetic changes – modifications in gene activity that occur without changes in the DNA sequence. These alterations impact critical components of skin health, like collagen production. Key enzymes, DNA methyltransferase 1 (DNMT1), histone deacetylase 4 (HDAC4), and Enhancer of zeste homolog 2 (EZH2), play significant roles in this process. By understanding and potentially reversing these changes, novel strategies for skin aging prevention and treatment can be developed.

Skin aging is a complex biological process involving intrinsic aging, a natural, inevitable process, and extrinsic aging, primarily caused by environmental factors such as ultraviolet (UV) radiation. Recently, epigenetic alterations, which affect gene expression without modifying the underlying DNA sequence, have been identified as pivotal regulators of skin aging processes. UV radiation induces several epigenetic modifications and alters the epigenetic landscape of skin cells, influencing the regulation of genes vital for skin health and contributing to skin aging.

A significant player in the epigenetic regulation of skin aging is DNA methyltransferase 1 (DNMT1), an enzyme responsible for maintaining and creating new DNA methylation. UV radiation upregulates DNMT1 expression, leading to hypermethylation of the tissue inhibitor of metalloproteinase 2 (TIMP2) gene, effectively silencing its expression in UV-exposed human skin. Given that TIMP2 inhibits the breakdown of the extracellular matrix, this UV-induced hypermethylation significantly contributes to the aging process (J Dermatol Sci 2018;91:19-27).

Simultaneously, UV radiation leads to a decrease in type I procollagen production, that involves DNA methylation and histone acetylation in the COL1A2 gene promoter in human dermal fibroblasts. Further investigation of the epigenetic mechanisms behind this collagen production reduction has shown that UV radiation induces a decrease in histone acetylation in the COL1A2 gene promoter. This reduction is mediated by a decrease in the recruitment of p300, a histone acetyltransferase, and Smad2/3, key molecules in the TGF-β/Smad signaling pathway, to

the COL1A2 promoter. At the same time, UV radiation induces DNA methylation in the same region, another mechanism to suppress gene expression. The inhibition of this UV-induced DNA methylation with substances like anacardic acid, or a DNA methyltransferase inhibitor (5-AZA-2'-deoxycytidine) results in an increase in histone acetylation in the COL1A2 promoter, leading to an increase in type I collagen production (J Invest Dermatol 2017;137:1343-1352). Similarly, palmitoyl-KVK-L-ascorbic acid conjugate has shown potential to improve matrix abnormalities associated with skin aging through epigenetic regulation (J Dermatol Sci 2021;101:214-217).

A more detailed examination of histone acetylation shows that UV irradiation increases histone acetylases (HATs) activity but decreases that of histone deacetylases (HDACs). Specifically, UV exposure significantly reduces histone deacetylase 4 (HDAC4) expression, resulting in upregulation of matrix metalloproteinase 1 (MMP-1) and a downregulation of type I procollagen. The HDAC4 reduction could activate c-Jun N-terminal kinase (JNK), leading to an increase in MMP-1 and a decrease in type I procollagen, both of which contribute to the appearance of aged skin. Intriguingly, HDAC4 has been associated with cellular senescence. Overexpression of HDAC4 has been found to rescue the senescent cell phenotype through the regulation of the DNA damage-inducible transcript 4 (DDIT4), a senescence-associated factor. This discovery suggests a promising target for reversing cellular senescence, a state of irreversible cell cycle arrest contributing to aging (J Dermatol Sci 2021;101:107-114; Aging 2022;14:4653-4672).

Recently, enhancer of zeste homolog 2 (EZH2), a histone methyltransferase, has been identified as playing a dual role in the epigenetic regulation of skin aging. This enzyme, also upregulated by UV radiation, simultaneously increases MMP-1 expression and decreases type I procollagen expression, thereby exacerbating skin aging. Inhibiting EZH2 has been proposed as a potential anti-aging strategy to prevent UV-induced skin aging (Matrix Biol 2023;119:112-124).

In summary, extensive research underscores the vital role of epigenetic mechanisms in skin aging, particularly in response to UV radiation. Targeting these mechanisms, such as inhibiting EZH2, upregulating HDAC4, or modulating DNA methylation, could potentially yield novel strategies for preventing or mitigating skin aging.

Impacts of blue light on skin aging, pigmentation and epidermal metabolism

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Blue light, as high-energy shortwave light, is part of the visible spectrum with the highest frequency and highest energy.

Background

Blue light reaches the dermis and even deeper layers of the skin with a strong penetration force greater than UV, and has a long-lasting effect on the skin. Similar to the phenotypic and functional skin damage caused by UV exposure, blue light has some biological effects on the skin. Blue light exposure is inevitable in daily life, and the accumulation of blue light from natural light and artificial light devices can lead to skin barrier dysfunction and exogenous aging characteristics of the skin such as deep wrinkles and skin relaxation. In addition to causing skin barrier dysfunction and photoaging, blue light exposure may also cause a skin itch, but there are few reports on the relationship between blue light and skin sensation.

Aims

Our research uses blue light as an environmental exposure factor to explore the genetic mechanism of skin phenotype differences and the molecular mechanism of phenotype formation after skin response to blue light. The research can provide theoretical guidance for precise skin health care and a scientific basis for the prevention and control of related skin problems.

Methods

A total of 73 subjects were included in the study to evaluate skin function changes after blue light irradiation, as well as a sensory questionnaire survey. Also,a blue light mice model and a skin cell model were established for studying functional differences and molecular mechanisms.

Results 1

Our group observed the effect of blue light on skin barrier function through human clinical trials, mice experiments, and cell experiments, and found that high-energy blue light can cause the loss of water in human skin. And this phenomenon is more obvious in mice. After exposure to blue light, the skin of mice can exhibit phenotypes of skin barrier damage such as roughness, desquamation, and epidermal

thickening. At the same time, the functional proteins FLG, KRT1, and KRT10 of the mice's skin barrier are upregulated and abnormally located. The expression of KRT1, KRT10, KRT14, FLG, IVL,and LOR in skin cells was also upregulated ($p<0.05$)

Results 2

We investigated the mechanism of skin photoaging induced by blue light irradiation by establishing a mice blue light photoaging model and a cell model. In the study, it was found that continuous exposure to low-dose blue light in mice can cause a decrease in skin collagen and elastic fibers. In the following skin cell experiments, it was verified that blue light inhibits collagen expression by inhibiting the TGF-β pathway, and blue light activates the JNK/AP-1 pathway to upregulate MMP1 expression, which may further inhibit collagen expression, revealing the molecular mechanism of blue light-induced skin photoaging phenotype.

Results 3

We found that the TRP family may be involved in the process of blue light-induced skin itch, and the specific regulatory role still needs further research.

Conclusion

High-energy blue light damages the skin barrier, which may be related to the increased expression of skin barrier function-related proteins induced by blue light. Blue light also may induce skin aging through multiple molecular pathways TGF-β pathway and the JNK pathway. In addition, TRPV4 can be activated by blue light, which will further causeskin itch.

Keywords

Blue-light exposure, skin barrier, skin aging, skin itch.

Phototherapy in Egypt, opportunities and challenges

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Phototherapy has been practiced in Egypt for more than 75 years, starting with Broad-band UVB and PUVA (psoralen being introduced to the world by Prof El-Mofty in 1948) followed in the mid 90s by Narrow-band UVB (NB-UVB) and excimer laser/lamps since the beginning of the millennium. NB-UVB is the mainstay for vitiligo and most psoriasis cases, PUVA is mainly kept for mycosis fungoides and few psoriasis cases, while excimer is reserved for localized conditions.

In the last decade, the availability of machines as well as knowledge and awareness by doctors and patients have increased tremendously, thanks to the continuous training courses. There is a big network of governmental hospitals as well as private clinics who provide NB-UVB, broad band-UVA and excimer lamps at affordable prices. Providers are listed and circulated among dermatologists to facilitate a place as close as possible to the patient's residence. Patients are covered by governmental as well as private insurance.

Phototherapy sessions are given mostly twice weekly, usually combined with topical and systemic therapy. In our dark skin types (III-V) the long-term side effects (apart from photoageing) are very scarce.

Our challenges rely mainly on the progressive increase in the cost of the lamps, especially with the continuous devaluation of our currency. The decreased availability of imported goods (lamps, spare parts, new machines) in the last year, during the global turmoil, is an added problem.

Challenges encountered with patients include getting bored of the frequent visits, getting burned especially in summer months, patients living in distant areas away from all services and the lack of proper registries.

Another challenge was added during the COVID-19 pandemic, when all "unnecessary services" like phototherapy were stopped, resulting in disease relapse in many patients.

Trying to overcome these confronts and finding solutions for them represent the biggest challenge and the pushing force for dermatologists to continue this indispensable dermatologic service.

Practical questions in phototherapy that need to be answered

Phototherapy has been shown to be an effective treatment for many dermatoses.

Nevertheless, many questions remain unanswered for both patients and practitioners.

The aim of my presentation is to raise some questions that need to be answered regarding the real risk of skin cancer in dark-skinned individuals, the maximum allowed dose and sessions in phototherapy, the fact that globally there is less supervision from dermatologists for phototherapy units, how to minimize PIH postphototherapy in dark skin, whether there is any advantage for maintenance therapy in narrow-band UVB and other questions also.

Finally, I will be presenting some practical tips from my 25-year experience using phototherapy units.

A review of phototherapy practices in the Philippines

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For many skin illnesses, phototherapy is still an essential treatment option. It is versatile, cost-effective, and has a known long-term safety record.

Different modalities are available, including narrowband ultraviolet B, oral or topical psoralen plus ultraviolet A, and excimer lamp. Data was gathered from two tertiary hospitals in Metro Manila. The available modalities are narrowband ultraviolet B, oral and topical (bath and hand/foot soak) psoralen plus ultraviolet A, and excimer lamp. Of these, narrowband ultraviolet B is by far the most frequently utilized modality, while psoriasis is the most common indication. Staring doses are typically determined based on the Fitzpatrick skin phototype. Filipinos, which comprise the vast majority of patients seen at the phototherapy centers, are classified as Fitzpatrick skin phototype IV. Based from the Philippine Dermatological Society Phototherapy Directory, as of 2021, there are a total of 46 phototherapy centers nationwide and for many of these centers, narrowband ultraviolet B is the only modality available. Of the 46 phototherapy centers, more than half are concentrated within the metropolis, leaving far-flung provinces underserved. In addition, given the long-term nature of many skin conditions requiring phototherapy, the cost of therapy is an important consideration. For the majority of Filipino patients, healthcare expense is paid out-of-pocket as many do not have insurance or health maintenance organization (HMO) benefits; however, for those who do have insurance, coverage for phototherapy is variable with most cases having limited or no coverage. Despite this limitation, many patients are able to comply with 2-3 times weekly sessions. As the only medical specialty with the skills to supervise phototherapy administration, improving access to it and ensuring that it is always available to our patients are both parts of our initiative.

Usefulness of a digital medical device to optimise the effectiveness and safety of daylight PDT: an observational, multicentre, clinical practice study

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Actinic keratoses (AKs) are common skin lesions that appear in areas that have received long-term exposure to UV radiation. The prevalence in adults over the age of 45 years in Spain is estimated to be approximately 25%[(1)]. Treatment is considered necessary because a certain fraction of these lesions, ranging from 0.60% in the first year to 2.57% over 4 years, progress to invasive squamous cell carcinoma[(2)].

Daylight Photodynamic Therapy (DL-PDT) is an efficacious treatment of actinic keratosis which is found to be less painful and more convenient than conventional lamp-based PDT (Morton 2015). However, daylight introduces uncontrolled variability, such as time of year, cloudiness, and sunscreen application, that can make delivering effective controlled treatment challenging. An innovative satellite-based system (SmartPDT) is the first scientifically validated[(3,6)] digital medical device (CE-marked Class 1) solving this. It can support clinicians in accurately planning and then monitoring in real-time the effective solar radiation doses received by a patient in real-time anywhere (for example at the patient's own home). The relevant solar doses monitored for DL-PDT are protoporphyrin IX (PpIX)-effective and erythema-effective (sunburn risk). We present the current results of an observational, multicentre, prospective clinical study on the use of this digital solution in clinical practice for DL-PDT which is ongoing in several hospitals and clinical practices in Spain.

Objectives

The primary objective of the study is to evaluate the effectiveness of DL-PDT when assisted by SmartPDT in the clearance of AK in clinical practice. Secondary objectives of the study include evaluating the satisfaction of patients and clinical staff in SmartPDT usability, evaluating the safety of SmartPDT use for DL-PDT and evaluating the incidence of relapses at 6 and 12 months after a DL-PDT session.

Materials and Method

An observational, multicentre, prospective study of clinical practice is being performed in Spain from January 2022 to December 2023. Clinical teams use a web-portal for monitoring either a hospital-based DL-PDT or a home-based DL-PDT performed by the patient using a dedicated smartphone app. The AK area severity index (AKASI) score is recorded at 3, 6 and 12 months of follow-up. Adverse treatment reaction and patient photos are also digitally recorded. The treatment protocol being followed is defined in the European consensus paper[(7)] with appropriate modification for Iberian environmental and geographical conditions[(8)] using either aminolevulinic acid or methyl aminolevulinate as the photosensitizer and a sunscreen with a protection factor of at least 30. Patient selection inclusion criteria include having five or more AK lesions on face and/or scalp with Olsen grade I or II. Exclusion criteria include hypersensitivity to the relevant photosensitizer, those with porphyria or skin cancer in the treatment area, and any patients who have received treatment for their AK during the preceding 6 weeks.

Results & Discussion

So far 24 patients have been included, 4 females and 20 males, with ages ranging from 42 to 87 years old. Eighteen DL-PDT sessions have been performed, all successfully completed. In four of the sessions, patients used the app autonomously, in one session they were assisted in using the app, and the other sessions the patient was fully assisted by clinic staff and no app was used, only the staff web portal for monitoring doses. PpIX-effective solar doses over all administered treatments ranged from 8.4 J/cm² to 23.8 J/cm² (mean 13.0 J/cm²). All recorded treatments exceeded the protocol recommended minimum dose of 8 J/cm². Treatment times ranged from 1 hr 50 min to 3 hr 50 min. In terms of safety of exposure, erythemal-effective doses ranged from 2.1% to 69% of patient's MED, with a median of 8.4% (the doses given account for the spectral transmission of the specified sunscreen). No patients exceeded the recommended maximal exposure dose of 70% of MED. The average air temperature during the sessions ranged from 11.6°C to 22.0°C, treatment is not recommended below 10°C. AKASI score recorded immediately prior to treatment was (mean ± std. deviation) 4.02 ± 1.57 and post-treatment was 1.58 ± 0.90. A positive outcome of a reduced AKASI score was recorded for all patients. All patients suffered a mild or moderate reaction to the treatment which is typical for DL-PDT. From the data to date, no significant correlation is found between the PpIX radiation dose received and the change in AKASI score ($p>0.05$).

Conclusion

SmartPDT can help dermatologists to optimise the overall management and effectiveness of DL-PDT, planning and monitoring the real PpIX-effective and erythemal solar doses received by each patient as well as giving support for a more comfortable treatment with higher therapy adherence.

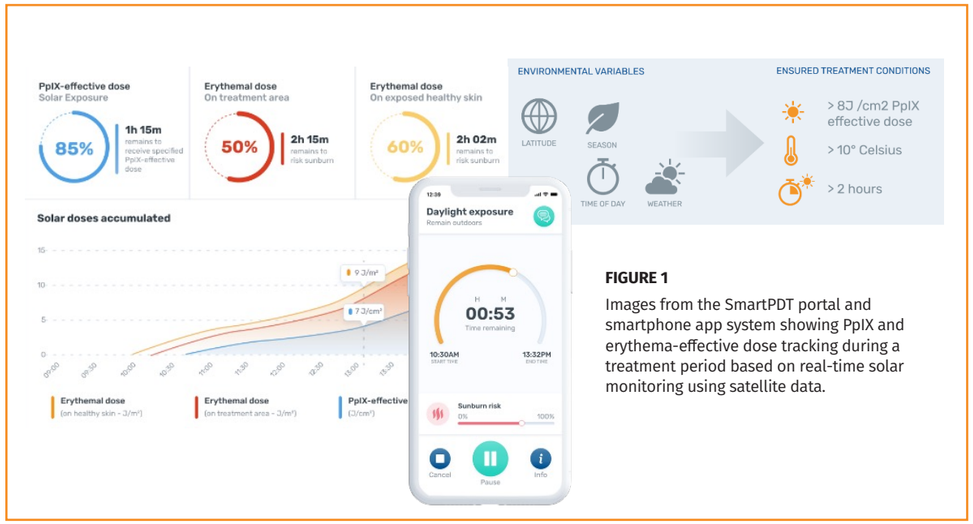
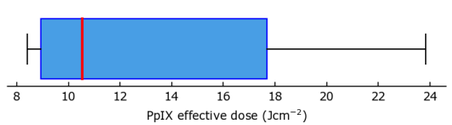


FIGURE 1

Images from the SmartPDT portal and smartphone app system showing PpIX and erythema-effective dose tracking during a treatment period based on real-time solar monitoring using satellite data.



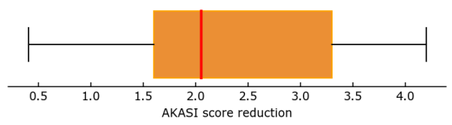


FIGURE 2

Left: Combined statistics of PpIX-effective dose. All recorded doses exceed the protocol minimum requirement of 8 J/cm^2.

Right: Reduction in AKASI score from pre-treatment to post-treatment assessment. All patients show a positive clinical response to the treatment. Red bar indicates the median value, whiskers indicate the range.

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590 LEDs Irradiation improved erythema through inhibiting angiogenesis of human microvascular endothelial cells and ameliorated pigmentation in melasma

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With the growing application of light-emitting diodes (LEDs), photobiomodulation and its therapeutic effect on melasma has aroused great interest. The pathogenesis of melasma is still uncertain, while abnormal vascular endothelial cells may play a role. We previously demonstrated LEDs yellow light could inhibit melanogenesis through melanocytes and keratinocytes. However, the mechanism of LEDs photobiomodulation on vascular endothelial cells as well as the effect of LED treatment on melasma remains unknown.

Objectives

To elucidate the possible mechanisms of 590 nm LEDs on the function of human microvascular endothelial cells (HMEC-1).

Materials and Method

HMEC-1 was irradiated by different doses of LEDs 590 nm. Cell counting kit-8 and apoptosis detection kit were used to detect cell viability and apoptosis. Scratch test and tube formation assay were performed to investigate cell migration and tube formation. Rt-PCR and ELISA was used to detect the expression of angiogenesis and melanogenesis related factors. The AKT/PI3K/mTOR signaling pathway was detected by western blotting in HMEC-1 after irradiation and the pathway agonist IGF-1 pretreatment.

Results

0-40 J/cm^2 LEDs 590 nm had no toxic effect on HMEC-1. Cell migration was decreased by 20 J/cm^2 and

40 J/cm² LEDs 590 nm irradiation, and tube formation capacity was inhibited after irradiation with 20-40 J/cm² LEDs 590 nm. The synthesis and the secretion of vascular endothelial growth factor-A and stem cell factor of HMEC-1 were downregulated after irradiation, and the inhibitory effect was most obvious at 20 J/cm². LEDs 590 nm inhibited the phosphorylation of AKT/PI3K/mTOR pathway in HMEC-1. After 50 ng/mL IGF-1 pretreatment, the inhibitory effect of LEDs 590 nm on cell migration and secretion of VEGFA could be reversed in HMEC-1.

Conclusions

LEDs 590 nm could inhibit HMEC-1 migration, tube formation as well as synthesis and secretion of VEGFA and SCF. LEDs 590 nm inhibited AKT/PI3K/mTOR pathway in HMEC-1 and reduced cell migration and VEGF secretion of HMEC-1 partly through AKT/PI3K/mTOR pathway. Our research provided new insights into the mechanism of PBM which has direct or indirect effect on melanocytes.

Sun exposure and photoaging are associated with sex-specific patterns of epigenetic, biological and mitotic aging in dermal and epidermal skin

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Sun exposure is an established risk factor for aging and skin cancer, and has been shown to induce widespread epigenetic changes in skin, overlapping with those found in squamous cell carcinoma and colorectal cancer[1]. Epigenetic modifications such as DNA methylation are dynamic across the lifespan and are known to reflect the impact of aging and external factors on the regulation of gene expression, serving as an interface between genes and environmental exposures[2]. Recent computational advances have enabled the inference of biological age, stem cell division rate and telomere length based on a tissue's DNA methylation profile. Aberrations in these metrics reflect dysregulated aging processes and have been implicated in age-related molecular changes and human disease[3,4].

Aim

This study investigated the role of DNA methylation-based aging algorithms in predicting the deleterious impact of sun exposure in a sex- and tissue-specific manner by leveraging a publicly available dataset based on the Illumina HumanMethylation450 microarray platform.

Methods

A clinical cohort of younger individuals aged <35 (n=10; mean age 26.6 ± 4.5 years; 5 female, 5 male) and older individuals aged >60 (n=10; mean age 73.9 ± 8.8 years; 6 female, 4 male) composed of dermal and epidermal skin derived from sun-exposed and sun-protected regions (total n=78) was interrogated for eight DNA methylation-based algorithms that predict epigenetic age (Horvath5, Skin&Blood6, Hannum7), biological age (PhenoAge18, PhenoAge29), telomere length (DNAmTL10) and cancer-linked mitotic age (epiTOC211, MiAge12).

Methylation-based age calculations for the above algorithms were generated using the methylCIPHER R package13. Association between methylation-based age and chronological age was assessed using Pearson product-moment correlation. Epigenetic and biological age, as well as telomere length dysregulation (acceleration or deceleration) was defined as the mean group-wise difference in residuals derived from the linear regression of calculated measures of chronological age. Mitotic age was reported as total number of stem cell divisions (TNSC) and stem cell divisions per year (SCDR, calculated as TNSC/chronological age). Analyses were further stratified by tissue (dermis and epidermis), sex and sun exposure to assess for differences in methylation-based age dysregulation, and for associations between age dysregulation and two measures of photoaging (the Griffiths14 and Helfrich15 photoaging scales).

Results

We observed strong, significant positive correlation between chronological, biological and mitotic age (R=0.60~0.98, p=0.0031~2.2x10-16) and negative correlation between chronological age, telomere length and epiTOC2-SCDR (R=-0.33~-0.42, p=1.1x10-4~3.9x10-9) in our cohort, demonstrating the ability of tested algorithms to predict age. Further, we identified overlapping but distinct patterns of methylation-based age dysregulation in sun-exposed versus sun-protected skin in dermal and epidermal samples across both younger and older age groups. By and large, epigenetic age was significantly ($p<0.05$) decelerated (Younger-Dermis Horvath, PhenoAge, Hannum; Older-Dermis Horvath, Skin&Blood, Hannum; Younger-Epidermis PhenoAge2, Hannum; Older-Epidermis Horvath, Skin&Blood, PhenoAge), and telomere length was reduced (all groups except Older-Dermis) in sun-exposed versus sun-protected skin. In the Older-Epidermis group, we also observed significantly ($p<0.05$) higher mitotic age (MiAge), including both TNSC and SCDR, in the sun-exposed versus sun-protected group.

This trend was also observed in sex-stratified analyses, occurring more frequently in female-derived skin. This included significantly ($p<0.05$) reduced epigenetic and biological age, as well as telomere length in exposed versus protected skin in both younger and older groups, as well as in dermal and epidermal tissue, versus male counterparts (only significantly observed in younger dermal and older epidermal skin). Among male-derived skin in the Younger-Epidermis group, we also observed significantly ($p<0.05$) greater epiTOC2-SCDR in sun-exposed versus sun-protected skin.

Stratifying by sun exposure and age group, we observed significantly ($p<0.05$) higher Horvath and DNAmTL and lower Skin&Blood, PhenoAge1&2 and Hannum measures of methylation-based age dysregulation in dermis versus epidermis across all tested groups. Further, stratifying by sun exposure and tissue, we observed significant negative correlation between photoaging and PhenoAge2 in both sun-exposed dermis (Griffiths-PhenoAge2 R=-0.682, $p<0.001$; Helfrich-PhenoAge2 R=-0.712, $p<0.001$) and epidermis (Helfrich-PhenoAge2 R=-0.564, $p<0.05$), but not in sun-protected tissue.

Conclusion:

We report several measures of methylation-based age dysregulation in response to sun exposure in both dermal and epidermal skin, more frequently occurring in female-derived, epidermal and sun-exposed samples. Notably, we report that sun exposure is associated with epigenetic and biological age deceleration, increased total number of stem cell divisions and reduced telomere length, with biological age being strongly negatively associated with skin photoaging. Our findings may be reflective of

01. Cellular and molecular changes associated with altered genomic regulation as a product of sun exposure,

02. Sex differences in sun exposure and skin protection,

03. Epigenomic differences between dermal and epidermal tissue, and

04. Methylation-based photoaging effects on sun-exposed skin. Our findings may have relevant links to the development of age-related skin diseases and predisposition to skin cancer.

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Comparision between NB-UVB only treatment and combination of NB-UVB with a topical cream comprising superoxide dismutase, reductase, and catalase in vitiligo

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Vitiligo is an acquired depigmentation illness that affects one percent of the population. The most cases start from young age and adolescent. The most popular treatment options for vitiligo are photochemotherapy and surgical procedures, but they come with several short- and long-term negative effects[(1)].

Although psoralen phototherapy (psoralen ultraviolet A (PUVA)) is still the most common treatment for vitiligo, it is limited in its use due to side effects such as nausea, phototoxic responses, cataract risk, and long-term carcinogenic risk. Narrow-band ultraviolet B (NBUVB) therapy has recently been reported to be an effective and safe treatment option for vitiligo patients[(2,3)]. SOD complex (superoxide dismutase, reductase catalase) from the Saccharomyces cerevisiae yeast - Dismutin BT. This complex has a detoxifying action with anti-radical properties[(4)] that can stimulate the general metabolism of the cells [Chambon *et al.*[(5)]]. In our study we compared combined topical cream containing superoxide dismutase, reductase catalase with NB-UVB to NB-UVB only treatment.

Methods

40 patients with vitiligo affecting the face and neck with or without involvement of the rest of the body between 18 and 60 years of age who came to the Physical Treatment Department of Dermatology, National Dermatology Center of Mongolia between April 2020 and June 2021 (20 in each group) were included in the study, while patients with pregnancy and lactation, history of photosensitivity, history of any immunosuppressive disorder or use of immunosuppressive medicines were excluded. The informed consent of the patients who were chosen was acquired. The patients' hospital registration numbers were kept on file. Each patient underwent a thorough medical history and physical examination, which included a skin examination in which the distribution of vitiligo patches was demonstrated and evaluated using the Wood's lamp. topical was categorized as segmental or non-segmental based on the pattern of patch distribution. The willingness to use topical cream was used to assign patients to each group. Patients in treatment group A was given topical cream containing superoxide dismutase, reductase catalase while group B only received narrow band phototherapy.

Both groups received concurrent NB-UVB therapy three times per week, starting at a low dose of 0.3J/cm^2 and gradually increasing by 10% with each session. Patients were told to report any side effects they experienced during therapy, such as burning, itching, or erythema. When a previous treatment resulted in severe erythema, the next session's phototherapy was skipped or the dose was reduced in accordance with the symptoms. Treatment with the same dose was considered suitable for light erythema. Treatment response was calculated monthly for three months and expressed as a percentage of depigmentation. On initial visit total area of face and neck was calculated by VASI score. The percentage of depigmentation was reviewed by VASI score on future visits. To ensure follow-up, the patients' addresses and phone numbers were recorded.

2. Data analysis and statistics

SPSS version 21.0 was used to analyze the data. At baseline, numeric variables such as age and % depigmentation were described using mean and standard deviations. Gender, disease duration, vitiligo type, and response were all categorical variables that were described using frequencies and percentages. Significant was defined as a P value of less than 0.05.

Results

The mean age in group A was 32.1 years and that in group B was 29.40 years. Both groups had a male-to-female ratio that was similar. The duration of the disease was less than 3 years in the 60% of the participants. Group A had a current depigmentation percent of 8.60 (standard deviation 4.684). Group B had a current depigmentation percent of 13.0 (standard deviation 7.588). It was statistically significant to analyze the percentage of baseline depigmentation and the percentage of current depigmentation in SPSS 21. ($p < 0.001$) The correlation coefficient for each group are 0.899. and .973, respectively. Sig. (2-tailed) = 0.00 <0.05, so the correlation coefficient is statistically significant.

Conclusion

The goal of this study was to propose a new therapy option that could be useful to vitiligo patients. It may also result in rapid symptom relief, reducing psychological distress caused by vitiligo-related cosmetic deformity, particularly on the face and neck. We have concluded that compared to NB-UVB only treatment, a combination of NB-UVB with a topical cream comprising superoxide dismutase, reductase catalase is more effective.

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Photodermatoses in Indian skin type: an analysis of disease spectrum; its association with Minimal Erythema Dose (MED) for NBUVB and UVA

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BACKGROUND

Minimal erythema dose or MED is the just perceptible erythema observed after 24 hours of irradiation. In patients with photodermatoses, we expect the MED to be lower than the general population; there is paucity of data about the spectrum, morphology and MED of photodermatoses in ethnic skin type (Fitzpatrick Type IV and V).

Objective

To study the spectrum, morphology and MED in photodermatoses patients with darker phenotypes.

Patients & Methods

Fifty patients with a suspected diagnosis of photodermatoses with lesions in photo-exposed parts of the body and/or photosensitivity were included in the outpatient department during the period of November 2013 to March 2015 after institutional ethical clearance. The history and morphology were noted and phototesting with ultraviolet A (UVA) and narrowband ultraviolet B (NBUVB) was done after informed consent. Patch and photo-patch test were done for suspected photoallergic dermatitis and chronic actinic dermatitis wherever indicated.

Results

The most common dermatoses seen were Polymorphic light eruption (PMLE), followed by hair dye dermatitis and Discoid lupus erythematosus (DLE). Type IV skin was seen in 37 patients (74%) while type V was seen in 13 patients (26%) (p value = 0.012). The study showed reduced Minimal erythema dose (MED) for UVA (20 J/cm^2) in 9 (18%) patients and reduced MED for NB-UVB (600 mJ/cm^2) in 5 (10%) patients. The total number of patients with reduced MED for both UV-A and/or NB-UVB were 11 (22%). Thirteen patients (26%) were patch and photopatch tested with Indian Standard series, in addition to being phototested. These included 8 patients of hair dye dermatitis, 2 patients each of chronic actinic dermatitis (CAD) and photosensitivity dermatitis and 1 patient of Airborne contact dermatitis (ABCD) with photoaggravation. Photo-augmentation of the patch test reaction occurred in three of patients with hair dye dermatitis for para-phenylene diamine (PPD). A negative patch test to 3 PPD but a positive reaction to “as is” sample of hair dye with photo-augmentation seen in some cases. The percentage of PPD used in the Indian standard battery may be insufficient to elicit an allergic reaction on patch test. One of these patients had a reduced MED to both UV-A and NBUVB. The limitation of the study was small sample size.

Conclusion:

The morphology and spectrum of photodermatoses differs in darker phenotypes. Even with protective melanin, there may be reduction in the MED leading to an abnormal cutaneous response manifesting as a photodermatoses. To our surprise, photoallergic hair dye dermatitis, associated with anecdotal reports of photosensitivity, had lower MED in comparison to other photodermatoses. We present here, PPD as an emerging photoallergen. Hence, hair dye manufacturers as wells as consumers must be sensitized regarding the various implication of PPD content in hair dyes.

Expanding photo-immunology into COVID - A randomized control trial

Abhimanyu Abhimanyu PhD, Andrew Dinardo MD PhD, Frank Lau MD, Prue Hart PhD, Richard Weller MD, Carmen Castilla MD

For over one hundred years, phototherapy has been used as treatment for a variety of conditions. more recently it has been used by dermatologists for inflammatory conditions; such as atopic dermatitis and psoriasis. our understanding of these inflammatory conditions has evolved over the years. these conditions are not just limited to cutaneous inflammation, they are actually systemic inflammatory diseases. It is easily forgotten that the skin is an organ with a reservoir of cells that communicate intimately with the systemic immune system. For this reason, UVB may be a non-invasive treatment option for systemic inflammatory diseases beyond its current dermatologic applications.

Historically, the connection between the skin and the systemic immune system was thought to be entirely mediated through vitamin D upregulation by UVB. Vitamin D serves as a prognostic indicator for many systemic inflammatory conditions and may play an important role in COVID-19. It is known that systemic immune dysregulation plays a role in COVID19 morbidity and mortality. Interestingly, population studies described a correlation between low environmental UVB exposure and increased COVID-19 morbidity, although large randomized controlled oral vitamin D supplementation trials have failed to provide clinical benefit. Yet, our understanding of the broader systemic effects of NB-UVB is evolving. There are parallel pathways initiated by UVB that are independent of vitamin D in the immune response. One such pathway upregulates circulating T-reg cells modulating systemic inflammation beyond the scope of vitamin D. We hypothesized that NB-UVB would engage the vitamin D independent, photo-immune cascade to stabilize the systemic immune system and safely improve COVID-19 survival. We present the results of our phase 1 randomized trial for high-risk COVID-19 patients along with their clinical and systemic response. Together these provide a window into the potential use of UVB for COVID-19 and its effects on systemic inflammation.

Objectives

To prospectively assess the safety and feasibility of adjunctive NB-UVB phototherapy in hospitalized, high-risk COVID-19 patients not requiring critical care.

Materials and Method

The Photo-Protection Trial is a prospective, double-blinded, randomized, placebo-controlled trial [NCT04818970]. Consecutive patients admitted with a positive COVID-19 PCR between May 24, 2021 and August 16, 2021 were screened for enrollment, concurrent with the intuition's IRB approval. Enrollment criteria included age between 50 and 95 years old, peripheral oxygen saturation <94% on room air and at least one comorbidity (obesity, hypertension, diabetes), admission < 3 days and the absence of exclusion criteria. Enrolled subjects were computer randomized 1:1 to NB-UVB (311nm) or placebo light. The treatment and placebo lights were identical FDA cleared phototherapy device, 1 Series Phototherapy Unit by Daavlin, with NB-UVB bulbs. The devices were mounted on customized rolling stands with battery packs. Visually identical UVB absorbing plexiglass was used on the placebo lights. There was weekly calibration by blinded non-study staff confirming placebo lights to have zero NB-UVB output. The initial NB-UVB dose was calculated according to skin type, based on the American Academy of Dermatology guidelines. Enrolled subjects were treated daily with NB-UVB accounting for residual UVB dose, or placebo light on 27% of their body surface area (BSA) for a maximum of 8 consecutive days. BSA was calculated based on the clinically accepted Wallace rule of nines. Standard of care therapies for COVID-19 were continued.

Blood samples were drawn at baseline and every 48 hours for assessment of immune stabilization and tested by Multiplex ELISA using the LegendPlex Human Inflammation Panel by BioLegend. This panel allows simultaneous quantification of 13 systemic inflammatory cytokines/chemokines, including IL-1β, IFN-α2, IFN-γ, TNF-α, MCP-1 (CCL2), IL-6, IL-8 (CXCL8), IL-10, IL-12p70, IL-17A, IL-18, IL-23, and IL-33.

The primary endpoint was mortality at 28-days. Secondary endpoints included biomarker assessment for immune stabilization as compared to baseline. The primary and secondary endpoints were assessed by Fischer Exact tests, paired t-tests or Wilcoxon signed rank tests as appropriate.

Results:

The randomization produced patient cohorts of 15 each, with similar demographics and mix of Fitzpatrick skin types. The placebo group had a trend toward more patients with partial or full vaccination. The average cumulative dose per treated patient ranged from 300 to 2,434 mJ/cm^2, with a median of 1,045 mJ/cm^2. Twenty-eight day follow up was completed for all 30 (100%) subjects.

The clinical primary endpoint was mortality at 28 days, 5 (33.3%) placebo patients died of COVID-19 hypoxia, vs. 2 (13.3%) treatment patients (p=0.19). A reduction in mortality was observed in unvaccinated, partially and fully vaccinated patients.

The secondary endpoints were assessed at baseline for all patients and in pairwise t-tests to their samples at 48 hours (9 in the treatment and 12 in the placebo cohort). Their baseline biomarkers had slight differences with statistically higher MCP-1 and lower TNF-α and IL-13 in the treatment group. The biomarkers had significant diversions from baseline at the 48-hour timepoint, which was performed after the third daily treatment. Stabilization of the inflammatory cytokines were observed in statistically significant decreases in IL-6, IL-8, IL-18, and MCP-1. It is noted MCP-1, a key pro-inflammatory macrophage chemokine, decreased by over 80% in this short period. Conversely, over the same timepoint, the placebo group recorded increased inflammation as measured by IL-23 and TNF-α and decreases in IL-10. Comparison across the cohorts, the placebo cohort had higher inflammation in IL-6 and MCP-1 at 48 hours. Vitamin D levels did not change. There were no phototherapy related adverse events in either arm.

Conclusions

In this pilot study, NB-UVB phototherapy in hospitalized COVID-19 patients was safe and easily implemented. Stabilization of the inflammatory cytokines were observed in statistically significant decreases in IL-6, IL-8, IL-18, and MCP-1. It is noted MCP-1, a key pro-inflammatory macrophage chemokine, decreased by over 80% in this short period. This provides evidence of NB-UVB's ability to modulate the systemic immune system independent of the vitamin D pathway. UVB has stabilizing effects on systemic inflammation and justifies further investigation into its clinical applications beyond dermatology.

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"Expanding Photo-immunology into COVID - a randomized control trial."

AUTHORS:
Frank Lau[1], Andrew Dinardo[2], Abhimanyu Abhimanyu[2], Prue Hart[3], Richard Weller[4] & Carmen Castill[5]

POSTER 2
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"Biological effects of sunscreen combined with self-tan on the function of ultraviolet radiation-exposed human skin equivalents."

AUTHORS:
Jessica Moor[1], Katy Foxcroft[2], Gillian Robson[2] & Mark Birch-Machin[1]

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