NEWS, VIEWS, AND REVIEWS

A Brighter Outlook for Photodermatoses: Emerging Adjuvant and Photoprotective Therapies

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INTRODUCTION

Photodermatoses are disorders characterized by abnormal cutaneous reactions to ultraviolet radiation (UVR) or visible light.[1] They are categorized as idiopathic, endogenous, or due to exogenous agents.[1] Idiopathic photodermatoses include polymorphic light eruption, juvenile spring eruption, hydroa vacciniforme-like lymphoproliferative disorder, actinic prurigo, chronic actinic dermatitis, and solar urticaria.[1,2] Among the idiopathic photodermatoses, polymorphic light eruption is the most common, with an estimated prevalence of 10% among the general population.[3] The pathophysiology is thought to result from UVR triggering immune dysregulation, resulting in autoimmunity and development of erythematous papules, vesicles, or plaques within hours of sun exposure with associated itch and/or burning.[2,4] Endogenous photodermatoses are inherently phototoxic disorders. They primarily comprise the porphyrias, which are genetic disorders in heme metabolism that lead to porphyrin accumulation. Upon UVR exposure, affected individuals may develop photosensitivity, crusted lesions, bullae, and scarring.[1,5]

Exogenous photodermatoses are classified as phototoxic or photoallergic reactions.[1] Phototoxic reactions occur when a drug or chemical absorbs UVR and directly damages skin cells, leading to exaggerated sunburn-like erythema, edema, or blistering.[1,6] Common causative agents include sparfloxacin, doxycycline, ciprofloxacin, voriconazole, hydrochlorothiazide, naproxen, and other non-steroidal anti-inflammatory drugs.[6] In contrast, photoallergic reactions are immune-mediated, delayed hypersensitivity responses that develop only in previously sensitized individuals.[1] A recent analysis of photopatch testing in 363 patients with suspected photoallergic contact dermatitis (PACD) identified a 20% PACD prevalence, with sunscreens containing benzophenones, antimicrobials, and fragrances as the most common allergens.[1] Key features of photodermatoses are summarized in Table 1.

Photodermatoses have substantial impacts on quality of life and daily practices such as clothing choices, employment, and social life, underscoring the need for adequate treatment.[7]

In the absence of standardized management guidelines, this review summarizes current photodermatoses therapies and highlights emerging preventive and treatment strategies.

Photodermatoses Management

Prevention

While sunscreens primarily protect against UVR by absorbing or reflecting radiation, formulations that combine physical filters, such as titanium dioxide and iron oxide, with DNA repair enzymes, including photolyase and endonuclease, enhance photoprotection in patients with photodermatoses.[1,8] Physical filters provide broad-spectrum UVR and visible light protection, while DNA repair enzymes help reverse UV-induced DNA damage.[1,8]

Oral and topical photoprotective adjuvants have gained attention for their ability to prevent UV damage and may benefit patients with photodermatoses. Polypodium leucotomos extract (PLE) is derived from the Polypodium leucotomos fern and has an extensive

Table 1. Key Features of Polymorphous Light Eruption, Solar Urticaria, Photoallergic Dermatitis, and Cutaneous Porphyria

Diagnosis	Onset	Duration of Lesions	Morphology	Distribution	Associated Features	Pathophysiology
Polymorphous Light Eruption	Hours to days after UV exposure[2,4]	Several days[4]	Monomorphic erythematous papules, vesicles, or plaques[4]	Neck, head, upper extremities, face often spared[2,4]	Pruritus, burning[4]	Delayed-type hypersensitivity reaction[2]
Solar Urticaria	Several minutes after UV exposure[18]	Resolves within 30 minutes to 24 hours after sun removal[18]	Urticaria, wheals, erythema[18]	Sun-exposed areas[18]	Pruritus , burning, systemic symptoms in approximately 10% of cases ie, nausea, headache[18]	Immunoglobulin E (IgE)-mediated mast cell activation in response to UVR[18]
Photoallergic Dermatitis	Hours to days after exposure to photosensitizer and UVR[19]	Days to weeks[20]	Eczematous dermatitis[19]	Sun-exposed areas[19]	History of topical photosensitizer[19]	Type IV hypersensitivity reaction[20]
Cutaneous Porphyria	Variable/chronic photosensitivity[21]	Weeks to months[21]	Blisters, erosions, scarring[21]	Sun-exposed areas; particularly hands and face[21]	Red/brown urine discoloration[21]	Porphyrin accumulation causing photosensitivity[21]

evidence base with human clinical trials demonstrating its role in photoprotection.[1,10,11] PLE exerts anti-inflammatory and antioxidant effects that counteract UV-induced damage, as it has been shown to increase the minimal erythema dose and reduce erythema intensity after a five-day course of PLE 250 mg twice daily.[1,9,10] It was also highlighted as an adjunct for actinic prurigo, demonstrating reduced disease severity and duration after one month of treatment at 15 mg/kg/day.[9] Additionally, antioxidant formulations containing vitamins C and E, ferulic acid, phenolics, or nanoformulated cannabidiol can reduce oxidative stress.[12,13,14] Topical cannabidiol has also been demonstrated to prevent UV-A-induced nuclear and mitochondrial DNA mutations.[14]

Treatment

Traditional treatment includes corticosteroids, phototherapy, discontinuation of offending agents, and treatment of underlying causes.[15] Topical or systemic corticosteroids may expedite resolution, while photohardening with UVB phototherapy, typically administered three to five times per week for 15–20 sessions, can promote light desensitization in advanced cases.[15] Additionally, thalidomide and hydroxychloroquine have long been used off-label for actinic prurigo, polymorphous light eruption, and solar urticaria.[1,16] In one report, thalidomide cleared pediatric actinic prurigo after seven weeks at 3 mg/kg/day.[1] Additionally, a multicenter study in Korea reported an 88.7% (n = 196/221) response rate in patients with unspecified photodermatitis after a median treatment of two weeks with hydroxychloroquine 200 or 400 mg daily.[16]

Biologics have been reported as emerging treatments for photodermatoses, although supporting studies are limited.[1] Omalizumab, an anti-IgE monoclonal antibody, has promoted remission in solar urticaria after four treatment courses of 375 mg every two weeks for six months, followed by 150 mg once monthly for three months.[1] Additionally, dupilumab, an interleukin (IL)-4 receptor antagonist, has been reported to achieve clearance of pediatric actinic prurigo after 8 weeks with 200 mg administered every two weeks, as well as adult actinic dermatosis after 12-16 weeks with 300 mg every two weeks.[1]

For erythropoietic protoporphyria, the US Food and Drug Administration (FDA) has approved subcutaneous afamelanotide, an α-melanocyte-stimulating hormone (α-MSH) analog, to extend the duration of time spent in direct sunlight without pain.[1,17] Afamelanotide induces skin pigmentation, enhances DNA repair, and promotes antioxidant defenses.[1,17] It has also been proposed as a potential therapy for idiopathic polymorphic light eruption; however, it has not yet been approved by the FDA for this indication.[8]

CONCLUSION

In the absence of established treatment guidelines, growing evidence supports a shift in the management of photodermatoses toward more personalized, multimodal approaches. Recent advances in photoprotective formulations, biologics, and oral supplements have broadened available therapeutic and preventive options for photodermatoses, enabling treatment to be tailored to patient comfort and preferences.

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