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Exploring the Gut Microbiome's Role in Drug-Induced Photosensitivity: A Need for Deeper Investigation

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INTRODUCTION

Drug-induced photosensitivity is an adverse reaction to ultraviolet (UV) radiation triggered by medications like antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and psychotropics, with manifestations ranging from mild erythema to severe dermatitis.[1] While the pathophysiology typically involves the generation of reactive oxygen species (ROS) and subsequent DNA damage, emerging evidence suggests the gut microbiome may have a role in modulating these reactions.

DISCUSSION

Photosensitivity reactions can manifest as either phototoxic or photoallergic. Phototoxic reactions occur when photosensitizing drugs absorb UV radiation, generating ROS and presenting as an exaggerated sunburn. Photoallergic reactions are immune-mediated and involve initial sensitization, during which the photosensitizing drug binds to proteins. Upon UV re-exposure, a hypersensitivity reaction resembling dermatitis occurs.[1]

These reactions can severely impact quality of life, often requiring sun avoidance, medication adjustments, and cancer risk management. Complex drug interactions, individual susceptibilities, and environmental factors complicate prediction and management. Research suggests the gut microbiome's influence on drug metabolism and immune response may be another variable affecting photosensitivity.[1]

The gut microbiome plays a key role in modulating drug pharmacokinetics and pharmacodynamics. Tsunoda et al demonstrated that gut bacteria can metabolize drugs and modulate host enzymes, such as cytochrome P450, impacting drug disposition and therapeutic outcome. The vast diversity of gut microbiota may help explain differing levels of drug-induced photosensitivity.[2]

The gut microbiome's impact on drug bioavailability is particularly evident in its interaction with NSAIDs. Certain gut bacteria produce the enzyme β-glucuronidase, which reactivates NSAID metabolites, leading to prolonged drug exposure and increasing side effects. However, research suggests modifying gut bacteria may mitigate these effects. Inhibiting β-glucuronidase in mice has been shown to protect against NSAID-induced intestinal damage.[2] Similarly, probiotics like *Lactobacillus gasseri* have reduced aspirin-associated mucosal breaks ($P<0.01$) and improved gastrointestinal symptoms in a cohort of 64 patients, while *Bifidobacterium breve* significantly reduced ulcers ($P=0.0258$) and aspirin-induced small-intestinal damage ($P=0.0376$) in 75 patients.[3,4] These findings underscore the importance of considering gut microbiota when addressing adverse drug reactions (ADRs).

The "gut-skin axis" highlights how gut microbiomes influence skin physiology and homeostasis through immune modulation and metabolic by-products. For example, gut-associated lymphoid tissues (GALTs), key to the innate immune system, produce antimicrobial peptides (AMPs) that regulate inflammation in the gut and skin. Dysbiosis, which disrupts GALT development, has been linked to skin conditions like atopic dermatitis and psoriasis, further reinforcing the gut-skin connection.[5]

Short-chain fatty acids (SCFAs), by-products of gut bacterial fermentation, also play a critical role in the gut-skin axis. SCFAs exhibit anti-inflammatory properties, strengthen the gut barrier, and may reduce skin inflammation.[5] In drug-induced photosensitivity, a well-balanced gut microbiome, producing sufficient SCFAs, may mitigate reaction severity by modulating the inflammatory response to UV-induced damage. Conversely, dysbiosis may exacerbate these reactions by promoting systemic inflammation and impairing the skin's reparative abilities. These insights suggest targeting the gut microbiome could serve as a therapeutic approach to managing ADRs.

CONCLUSION

Drug-induced photosensitivity remains a significant clinical challenge, with the gut microbiome's role in drug metabolism, immune function, and inflammation complicating its management. Research indicates gut health may influence the onset and severity of photosensitivity, offering the potential for microbiome-based therapies, including targeted probiotics. Further studies are needed to clarify the gut microbiome's role in photosensitivity and identify microbiome-targeted therapies.

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DISCLOSURES

The authors have no conflict of interest to declare.

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