Topical Treatment of Xeroderma Pigmentosum

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Ocular tumors also occur in patients with XP and particularly affect the eyelid, conjunctiva, and cornea, all of which are sun-exposed. The most frequently occurring eye neoplasm is SCC, which is followed by BCC, and, finally, by ocular melanoma.4 In patients with ocular disease, 50% of neoplasms occur by 11 years of age.4 Neurological abnormalities can also occur in this disease, manifesting as low intelligence and abnormal motor activity (ataxia and spasticity) as well as a slowed rate of growth.4

The skin cancers are essentially identical to the same types of skin tumors in patients without XP.2 Interestingly, in the normal population, 80% of BCCs and SCCs and 20% of melanomas occur in sun-exposed areas.5 In patients with XP, these frequencies increase to 97% for BCCs and SCCs and to 65% for malignant melanomas, respectively.5 Of note, there is an increased tendency for XP patients to have tumors of the anterior eye and tongue (generally the non-melanoma type) compared with the normal population.3

**Pathogenesis**

These frequencies of skin malignancies underscore the importance of UV irradiation in the pathogenesis of XP. Although UV irradiation is composed of both the ultraviolet A spectrum (320–400 nm) and the UVB spectrum (280–320 nm), UVB plays a more pivotal role in the etiology of XP.2,5,6 UVB is a known cause of photoaging, immunosuppression,7 and the formation of several photoproducts in DNA, the most important of which are called cyclobutane pyrimidine dimers (CPDs).2 CPDs are thought to be involved in the initiation of skin cancer.6

UVB-induced immunosuppression contributes to the formation of skin cancer because transformed cells are permitted to replicate.8,9 Patients with XP have a deficiency in DNA repair of UVB-induced damage. XP is a model genodermatosis, and eight different DNA repair genes have been implicated in this disease (XPA–XPG and XPV).5,8
useful therapeutic option, but it has been associated with DNA repair enzyme compared with the placebo group. A keratoses and BCCs was reduced in the group receiving the activity against CPDs.

First introduced more than 25 years ago into XP excisional repair of deficient cells to increase the rates of appearance of new actinic keratoses and BCCs were compared. The rate of development of new actinic keratoses and BCCs was reduced in the group receiving the DNA repair enzyme compared with the placebo group. A reduction of 68% was noted in new keratoses and of 30% in new BCCs. No adverse effects were noted in either group.

No increased serum immunoglobulin G (IgG) antibodies against the enzyme were detectable in any patients. It is significant that the reduced rates of occurrence were still noted six months after discontinuation of the medication, which is advantageous, in contrast to systemic retinoids. Continual application of the lotion throughout life was recommended, however, because people accrue sun damage as they age.

In another study, the sites in XP patients who were treated with the DNA repair enzyme liposomes had fewer CPDs and showed less erythema than the control sites did. No substantial changes in serum chemistry or dermatopathology were observed in the short term or over the long term in animals or humans. Further, no adverse drug reactions were observed in short-term or long-term safety testing in either mice or humans. The lack of systemic toxicity was explained by the fact that the enzyme remains localized in the epidermis.

Photolyase
Photolyase, another enzyme that repairs DNA, is found in fish, reptiles, marsupials, and plants but not in humans. Photolyase holds promise because it binds to CPDs specifically and removes them upon exposure of the complex to light. Wavelengths of 300 to 500 nm convert the pyrimidines back to their monomeric form. This mechanism of light-dependent DNA repair, called photoreactivation, has been reported to restore immune competence to UV-irradiated antigen-presenting cells.

In humans, photolyase (the 1% hydrogel formulation containing photolyase liposome is found in Photosome Daytime Formula) and light-treated areas showed increased DNA repair and protection against immune suppression, compared with sites without light exposure.

Conclusion
Both T4N5 and photolyase liposomal lotions are innovations in the therapy of XP. They look promising as adjuvant therapies in the management of XP, a devastating disease, incorporated alongside the current recommendations of the use of broad-spectrum sunscreens, and in conjunction with other sun-avoidance methods (e.g., wearing of a hat). T4N5 liposomal lotion has an advantage over sunscreen: unlike sunscreen, it is effective after UVB-induced damage to the skin has already taken place.

In the future, perhaps these enzymes might be delivered as genes that specifically code for the repair enzymes. We hope that larger clinical trials will be conducted to compare the efficacy of the two enzymes.
References


Disclosure

Drs. Lin and English have no financial relationships to disclose.
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