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Commentary

Clinical and Animal Studies in Photosensitizing Psoralen of Photo Carcinogenesis

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DESCRIPTION

In conjunction with suberythemagenic dosages, photosensitizing psoralen is a well-proven and extremely successful treatment for a variety of inflammatory skin conditions, including psoriasis, mycosis fungoides, and vitiligo. There is a known increased risk of Squamous Cell Cancer (SCC). This was initially hypothesised in animal models, and a lengthy prospective research known as the Psoralen Plus Ultraviolet-A Radiation follow-up study confirmed it to be a clinically meaningful connection. 1380 patients who received their initial systemic PUVA therapy for psoriasis in 1975 and 1976 were followed up on. They noticed a dose-dependently elevated risk of SCC that became apparent within 5 years of the initial exposure. In conjunction with suberythemagenic dosages, photosensitizing psoralen is a well-proven and extremely successful treatment for a variety of inflammatory skin conditions, including psoriasis, mycosis fungoides, and vitiligo. There is a known increased risk of Squamous Cell Cancer (SCC) associated with systemic PUVA. This was initially hypothesised in animal models, and a lengthy prospective research known as the PUVA follow-up study confirmed it to be a clinically meaningful connection. 1380 patients who received their initial systemic PUVA therapy for psoriasis in 1975 and 1976 were followed up on. They noticed a dose-dependently elevated risk of SCC that became apparent within 5 years of the initial exposure.

Azathioprine, a thiopurine analogue used in medicine as an immunosuppressant, makes human skin more sensitive to UVA light. Many inflammatory diseases, such as Crohn's disease, autoimmune disorders, and the aftermath of solid organ transplantation may benefit from long-term azathioprine treatment. The risk appears to be higher with immunosuppressive regimens that contain azathioprine, and the incidence of SCC is elevated in transplant recipients by an order of 65 to 250 times. A well-known photosensitizer called voriconazole is the first line of treatment for invasive aspergillosis. There are inconsistent results from studies examining the link between voriconazole use and Non-Melanoma Skin Cancer (NMSC). A large (n=467) retrospective US cohort study of adult lung and heart/lung transplant recipients found that although there was an association at the level of crude analysis, the association was diminished and not significant when confounding factors like patient gender, history of chronic obstructive pulmonary disease (possibly a surrogate marker for smoking status), and history of immune disorder were adjusted for. In contrast, a smaller US study (n=91) of lung transplant recipients at Emory University, Georgia, discovered that voriconazole use continued to be a significant risk factor for the onset of skin cancer even after accounting for all variables identified on univariate analysis as being significant risk factors for NMSC (longer time since transplantation, Fitzpatrick skin type, and history of sun exposure). Voriconazole use has been linked to an elevated incidence of melanoma *in situ* in one case series.

Using mouse models, researchers looked at the phototoxicity of the fluroquinolone antibiotic fleroxacin. They found that the phototoxicity was dose-dependent and those tumours, both malignant and benign, grew in the mice that experienced the most severe phototoxic effects. Another study using mice compared the photocarcinogenic potential of several fluoroquinolones (nalidixic acid, lomefloxacin, fleroxacin, ciprofloxacin, and ofloxacin) in the presence of chronic suberythemagenic UVA exposure, using 8-MOP as a positive control. The results showed that tumour development was significantly increased in all groups given a test substance compared to mice exposed to UVA alone in all cases. Unlike the fluroquinolone-treated groups, where the majority of tumours were benign, the lomefloxacin plus UVA group had a startlingly high rate of SCC, the majority of which were cystic, massive, and highly invasive.

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