COMMENTARY

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Has Vitamin D Had Its "Time In The Sun" For Melanoma?

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Abstract

Growing evidence suggests a pivotal role for vitamin D in cancers, particularly melanoma. The broad immunologic effects of vitamin D and its signaling axis make for a complex interplay between tumor cells and the immune system. Preclinical evidence suggests vitamin D to have protective effects in melanoma oncogenesis and progression, creating a potential role for vitamin D supplementation in cancer prevention and/or adjuvant therapy. In this commentary, the authors highlight studies of vitamin D in melanoma with clinical implications and call for large clinical trials to definitively determine the role of supplementation in patients to prevent and help treat melanoma.

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Vitamin D is obtained through dietary intake and produced in the skin by ultraviolet B conversion of 7-dehydrocholesterol into cholecalciferol, which is activated by CYP27A1 and CYP27B1.[1,2] Effects of vitamin D receptor (VDR) signaling include calcium-phosphate homeostasis, immune function, and cellular proliferation.[3,4] In certain cancers, vitamin D also demonstrates protective effects.[5–7]

Existing evidence demonstrates a clear role of the vitamin D axis in melanoma. VDR and CYP27B1 expression decrease with melanoma progression (increasing Clark level, Breslow's thickness, pTNM stage) and inversely correlate with metastatic potential.[8,9] Additionally, higher CYP27B1 and VDR expression is associated with improved overall and disease-free survival.[8,9] Small nucleotide polymorphisms (SNPs) within the VDR gene, the most well-studied of which are Taq1, Bsm1, and Fok1, have been associated with variations in melanoma risk.[10] Bsm1 has also been associated with multiple primary melanomas.[11]

Population-based studies of melanoma patients have shown low serum 25(OH)D3 levels to be associated with melanoma progression, poor prognosis, and lower survival.[12,13] *Post-hoc* analysis of the Women's Health Initiative calcium and vitamin D trial found supplementation did not reduce the overall incidence of skin cancer. However, women with prior nonmelanoma skin cancers had 57 percent fewer melanomas with supplementation versus placebo,[14] suggesting a protective role in high-risk patients. Nevertheless, this study is criticized for low supplementation (400IU daily), whereas current recommendations are 600 to 800IU with minimal toxicity at 4000IU.[15]

Although preclinical and observational studies confirm a role of vitamin D in melanoma, currently available evidence for supplementation in melanoma patients is not yet definitive. Large-scale, randomized, controlled trials of vitamin D supplementation in risk reduction and melanoma therapy with high dosing are necessary. Subgroup analysis of gene polymorphisms could also offer criteria for risk stratification and dosing. Taking this next step will make the promise of transitional science a reality for clinicians and their patients.

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