8 Vitamins and Micronutrients in Aging and Photoaging Skin

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CONTENTS

8.1 INTRODUCTION

Photoaging skin and skin cancer constitute a major problem in the U.S. as well as many other areas throughout the world. Natural aging of the skin is associated with many intrinsic changes. The addition of significant ultraviolet exposure creates the potential for benign photoaging changes as well as increasing the potential for skin cancers of all types including basal cell carcinoma, squamous cell carcinoma, melanoma, and a variety of others such as eyelid sebaceous carcinoma. While treatments exist for all types of skin cancers as well as surgical and nonsurgical treatments for photoaging changes (sagging, wrinkles, texture, pigmentation, etc.), prevention and the reduction of the incidence of malignant and nonmalignant conditions offer profound benefit for the individual and for society.

Evidence exists that the oral consumption, and in some cases the topical application, of specific fruits and vegetables or their components may play a role in the reduction of the incidence of both malignant and nonmalignant changes in the skin.

8.2 ULTRAVIOLET RADIATION

The ultraviolet radiation from the sun makes up only 6% of the nonionizing radiation (the remainder being infrared and visible). However, it does have the ability to penetrate the epidermis and induce photochemical reactions. Ultraviolet irradiation consists of UVA, UVB, and UVC. The ozone layer effectively absorbs UVC, leaving UVB and UVA to react with the epidermis. UVB is responsible for the redness, peeling, and burning related to sun exposure. UVB also damages cellular DNA and contributes to skin cancer. UVA penetrates deeper and contributes to both carcinogenic and nonmalignant (wrinkling, premature aging) conditions via a photosensitized reaction mediated in part by reactive oxygen species (primarily singlet oxygen). The subsequent free-radical formation damages not only the cellular skin components (proteins, fats, etc.) but also the genetic material(DNA/RNA). The nucleotide building blocks of cellular DNA absorb UV energy and are susceptible to mutagenesis, with a proportion becoming premalignant or malignant. The epidermal cells carry many UV-caused mutations, with the gene p53 having the highest prevalence (50%) of mutations of any human gene.[1] In its normal state the p53 gene protects the epidermal cell from tumor formation.

Immune suppression increases the risk of the development of skin tumors of all types including nonmelanoma skin cancer. The risk is also increased in AIDs patients. Benign photoaging changes are evident when one compares the facial cutaneous changes of sun-nonexposed and sun-exposed skin. This can be most dramaticaly envisioned by comparing the facial skin of a 60-year-old monk who never sees the sun with that of an American southwest Indian who is constantly exposed to ultraviolet irradiation.

Age-related macular degeneration (AMD) as well as cataracts are also related to UV exposure. AMD is the leading cause of blindness in people older than 65 (see Chapter 6: Fruit and Vegetable Micronutrients in Diseases of the Eye). Evidence suggests that nutrition plays a role in prevention and that two carotenoids (lutein and zeaxanthin) found in spinach may offer protection from AMD by absorbing damaging blue light as well as acting as antioxidants.[2] Nutrition may be important in skin cancer, as the Australians noted that an increased consumption of fish and vegetables, including the cruciferous vegetables (broccoli, brussels sprouts, cabbage, and cauliflower), correlated with a decreased incidence of skin cancer.[3]

8.3 VITAMIN C (ASCORBIC ACID)

Scurvy, the deficiency in Vitamin C characterized by skin hemorrhages, bleeding gums, fragile bones, and death, provides insight into our reluctance to recognize the power of nutrition. In 1753, British physician James Lind published his book *A Treatise of the Scurvy* detailing the cure and prevention via oranges and lemons.

Only in 1795, after Lind's death, did the British Navy adopt his work.[4] Vitamin C acts as an antioxidant in the skin by scavenging and quenching free radicals generated by UV radiation.[5] Dunham et al.[6] found reduced UV-induced tumors in mice given increased Vitamin C. Singlet oxygen formation has been found to be suppressed by antioxidant Vitamin C.[7] Wound healing is dependent on Vitamin C and this vitamin is essential for the production and stabilization of collagen. Older individuals may have lower Vitamin C levels[8] which may contribute to less than optimal cutaneous wound healing.[9,10] Supplemental Vitamin C for skin health should not exceed 1000 mg/day (taken in divided doses).

Topical Vitamin C has been studied both in prevention and treatment of photoaging skin. Forearms treated with 19% *L*-ascorbic acid solution showed reduction in redness as measured by the minimal erythema dose when compared to controls.[11] This protective effect may be related to the antioxidant properties of Vitamin C as it does not appear to offer absorption in either the UVA or UVB range. Topical 12% ascorbic acid solution penetrates the stratum corneum outer epidermis in 72 h,[12] with a 10% solution delivering pharmacologic levels. UV exposure was found to markedly decrease skin levels of Vitamin C in porcine skin.[13] In addition to promotion of its protective effects, multiple commercial preparations now promote restoration of skin tone, improvement in fine wrinkles, and a more youthful look as the positive cosmetic effects of topical Vitamin C.

8.4 VITAMIN E

Various studies evaluating the role of Vitamin E (alpha-tocopherol) both in the prevention of skin cancer, including melanoma, as well as evaluating plasma levels have produced conflicting results.[14,15] Thus, evidence supporting Vitamin E supplementation for skin cancer reduction needs further delineation. Interestingly, oral Vitamin E supplementation has been found to improve hyperpigmentation of the face.

Cultured human melanoma cells were evaluated for the inhibitory effect of alpha-tocopheryl ferulate (alpha-TF) on melanization.[16] Results were positive, suggesting that alpha-TF is a candidate for an efficient whitening agent via melanogenesis suppression and antioxidant function scavenging free radicals produced by UV radiation.

Topical Vitamin E is contained in many sunscreen products, either listed directly (i.e., tocopheryl acetate) or included in "other ingredients." Alberts et al. determined that while alpha-tocopheryl acetate was absorbed by the skin, it failed to undergo conversion to its unesterified free form which reduces UVB carcinogenesis.[17] However, improvement in wrinkle depth and length as well as skin roughness was noted following a 4-week application of topical 5 to 8% tocopherol cream to the face.[18]

Other antioxidants such as Vitamin C may be necessary to enhance tocopherol's photoprotective effects by preventing its degradation in the skin. Natural Vitamin E appears to be more bioavailable than synthetic forms when taken orally. Vitamin E seems to function as the major chain-breaking antioxidant in skin and other body tissues thus offering significant photoaging preventative effects. There appears to be a reduced risk of basal cell carcinoma with vitamin supplementation (including Vitamin E).[15]

Vitamin E supplementation orally for the skin should be at least 200 I.U. plus mixed tocopherols. Topical Vitamin E creams or gels in the *d*-alpha-tocopherol form (as opposed to the acetate form) should be applied every morning. The topical use of oil from capsules of Vitamin E may cause skin irritation in some patients.

8.5 VITAMIN A: RETINOL

Retinoids, including both natural and synthetic Vitamin A derivatives, provide a number of effects on the skin including regulation of both differentiation and growth in epithelial cells.[5] While the lower dosage of 10 mg/day of oral isotretinoin vs. placebo by Tangrea et al.[19] over 3 years failed to demonstrate any difference in reduction of new basal cell carcinoma skin cancers, Kraemer et al.[20] demonstrated that 2 mg/kg/day did provide reduction in the incidence of new nonmelanoma (basal cell and squamous cell) skin cancers. At our institution, patients with a history of multiple nonmelanoma skin cancers are routinely considered for prophylactic preventive oral isotretinoin therapy. Lippman et al.[21] found both advanced squamous cell carcinomas (71%) and basal cell carcinomas (51%) responded partially or completely to oral retinoids. Prolonged retinol supplementation in patients with actinic solar keratosis (precancerous lesions) was shown to increase plasma concentrations of multiple micronutrients and skin concentrations of retinol and retinyl palmitate.[22] Oral Vitamin A supplementation for the skin should not exceed 9000 I.U. daily.

Topical retinoids, namely trans-retinoic acid or tretinoin, have been shown by Kligman et al.,[24] Voorhees et al.,[25] and others [23,24] to decrease roughness, improve fine wrinkles, and lighten dark spots (lentigines) when applied to photodamaged skin. Side effects include dryness and irritation in some patients. Various other retinoids such as topical retinol, while weaker than retinoic acic, provide potent retinoid activity with low irritancy.[25]

In our practice, topical retinoid usage is a critical component of our photoaging topical regimen along with moisturizating regimens to combat dryness. Recently tazarotene, a new topical acetylenic retinoid, was shown to significantly reduce the mean minimal erythema dose (MED) for psoriatic skin exposed to UVB.[26]

8.6 CAROTENOIDS

Dietary beta-carotene, alpha-carotene, and cryptoxanthin are converted into Vitamin A. Beta-carotene was thought to reduce UV erythema but this study was not reproducible. Lutein and zeaxanthin, while related to beta-carotene, do not interconvert in the skin. In the eye, human macular pigment is composed of lutein and zeaxanthin which function as antioxidants as well as filtering and absorbing blue light.[27,28] It is possible that lutein and zeaxanthin could have a similar role on the skin. Sun exposure of as little as 1 h can cause a decrease in serum carotinoids.[29] Lee et al. showed that skin erythema after simulated solar radiation could be reduced with oral natural

carotenoid supplementation.[30] This is a most important finding as it opens the door for research on natural materials to protect the skin from UV irradiation.

We evaluated sun-damaged skin in patients with nonmelanoma skin cancer and found a sevenfold higher level of carotinoids, but not retinol, in the skin of the nose of one patient (total of six patients studied) with a similar distribution pattern in skin as in plasma but with much lower values than expected in all six cases.[31]

8.7 VITAMIN B

Biotin, niacin, and riboflavin are essential in normal skin functioning. Panthenol (Vitamin B_5) functions as a humectant, attracting moisture to the hair and skin.

8.8 VITAMIN D

Calcipotriene cream for psoriasis contains the same compound as the Vitamin D found in oral vitamin supplements. Vitamin D supplementation does not appear to be necessary in the majority of healthy individuals using sunscreens on a regular basis.[32] Skin covered with a topical sunscreen with an SPF of 8 or greater fails to produce Vitamin D. Intentional sun exposure is not the optimal way to increase Vitamin D levels in the normal healthy individual.

8.9 SELENIUM

This dietary trace element may play a role in decreasing the risk of nonmelanoma skin cancer.[33] As it is often obtained through seafoods along with omega-3 fats and Vitamins A and D,[34] this positive benefit may only partially be related to the selenium. Selenium supplementation should be in the range of 100 to 200 μg daily.

8.10 COENZYME Q10

Coenzyme Q10 (ubiquinone) functions in part as an antioxidant and has been promoted as a topical treatment to reduce the depth of facial wrinkles.[35] Poda and Packer suggest that coenzyeme Q10 is the first antioxidant to be reduced when there is oxidative stress to the skin.[36]

8.11 VITAMIN K

Historically, Vitamin K has been given orally preoperatively to patients undergoing cosmetic procedures, such as facelifts, to minimize bruising. One recent report touted the use of a topical Vitamin K (phytonadione 1%) and Vitamin A (retinol 0.15%) preparation to provide significant improvement (93% of patients) for the appearance of periorbital hyperpigmentation (dark circles under eyes).[37]

8.12 GREEN TEA

Polyphenolic epicatechin and epicatechin derivatives in green tea extracts reportedly inhibit UV irradiation-induced skin cancer in mice. This antioxidant protective property was demonstrated to be effective with either oral administration or topical application.[38] Interestingly, the Canadian Cancer Society is accepting requests for funding research for alternative cancer therapies, including green tea.

8.13 FATTY ACIDS

Essential fatty acid deficiency can manifest with erythema, dryness, and scaling of the skin. Skin changes lag behind plasma changes by several months. Fat may function as an immune suppressant, with foods high in polyunsaturated fatty acids increasing the risk of melanoma and even premalignant solar keratosis.[15] Omega-3 fatty acids, found in fish (albacore tuna, sardines, salmon, cod, and mackerel) may help block tumor growth.[39]

8.14 SUMMARY

Micronutrients, antioxidants, and vitamins assist in developing and maintaining healthy skin. They are important in reducing aging changes and providing a more youthful appearance. Protecting against free radicals which damage skin cells, antioxidants, vitamins, phytonutrients, essential fatty acids, and proper internal and external hydration help maintain a youthful skin. Future research will certainly explore the use of these substances to naturally protect the skin from solar radiation, both in terms of skin cancer prevention and in protecting and treating the benign photoaging effects so many of us seek to avoid or correct.

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