Cancer Epidemiology, Biomarkers & Prevention

Hypothesis/Commentary
Commentary on Yang et al., p. 683

Can UV Exposure Reduce Mortality?

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Abstract

A Swedish cohort analysis in this issue (1) demonstrates a significant reduction in all cause mortality and in cardiovascular mortality associated with several measures of sun exposure. In addition, ultraviolet exposure from tanning beds is associated with a significant increase in all cause mortality and cancer mortality. A potential explanation for the protective association is that UV exposure results in high levels of serum vitamin D which may improve survival. However, that explanation does not hold for ultraviolet exposure from tanning beds, which in this study is associated with a significant increase in all cause mortality and cancer mortality. Such a finding is curious and inconsistent with a vitamin D hypothesis. These results should impel investigators to study further the biology of ultraviolet radiation, both natural and artificial, and its health effects. *Cancer Epidemiol Biomarkers Prev; 20(4); 582–4. ©2011 AACR.*

Poison is in everything, and no thing is without poison. The dosage makes it either a poison or a remedy.

Paracelsus

Introduction

There has been much discussion in the literature as to the benefits and risks of UV exposure, both natural and artificial. The risks of excess UV exposure focus on skin cancer and the benefits on vitamin D. However, a very recent Institute of Medicine report (2) clearly states that "there is not sufficient evidence to establish a relationship between vitamin D and health outcomes other than bone health" and that the recommendations are based on minimal solar exposure (i.e., almost none). A new article in this issue of *Cancer Epidemiology, Biomarkers & Prevention* (1) demonstrates both beneficial and harmful effects from different forms of UV exposure—natural and artificial-–in a prospective study of 38,472 women in Sweden who were followed for 15 years. Among this group, 754 deaths occurred—457 from cancer and 100 from cardiovascular disease. Overall mortality was reduced among those who had been sunburned 2 or more times a year as teenagers compared with those who had been sunburned 1 or fewer times (HR = 0.7; 95% CI 0.5–0.9). In addition, overall mortality and CVD mortality was reduced (HR = 0.7, 95% CI 0.6–0.9; HR = 0.5, 05% CI 0.3–0.8, respectively) among those who had taken sunbathing vacations more than once a year during 3 decades. Conversely solarium use once or more per month for at least a decade increased the risk of all cause deaths compared with those who never used solaria (HR = 1.9; 95% CI, 1.3–2.7) as well as total cancer deaths (HR 1.6; 95% CI, 1.0, 2.8). The study has an excellent design (a prospective cohort), repeated measures of sun exposure and diet and is able to control for a number of potential confounders, such as pigmentation, BMI, education, and exercise. These results are likely to be controversial, but understanding their biological basis will be critical to evaluate the risks and benefits of UV exposure.

Due to the lack of strong data for the relationship between UV exposure and serum vitamin D, it is difficult to draw conclusions about the rationale for the effects seen in the Yang and colleagues paper (1) where 2 of multiple measures of sun exposure in a prospective cohort are associated with improved overall mortality and improved cardiovascular mortality. However, it should be pointed out that the lack of an association for these measures in relationship to cancer mortality is not inconsistent with varied studies to date, ecological, and prospective (e.g., 3). It may be that different measures than those used by Yang and colleagues are inversely associated with cancer mortality, such as solar elastosis and serum vitamin D (e.g., 4–6).

Intermittent UV and melanoma risk

Meta-analyses of the many studies conducted on the role of solar UV exposure and melanoma etiology are highly consistent and demonstrate an increased risk of approximately 1.6 for the development of melanoma with high levels of intermittent sun exposure (7–9). Within this cohort Veierod had previously found an increased risk between UV exposure, both natural and artificial, and the development of melanoma (10). Thus, the study itself is internally consistent with known effects of UV. Artificial UV exposure clearly increases risk for melanoma and

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nonmelanoma skin cancer (11) as has been demonstrated in ecological (12), case–control (13), and cohort studies (10). Conversely, it is well established that chronic sun exposure does not increase risk for developing melanoma although the mechanism for that observation is unclear (7–9).

Benefits from UV exposure

Although the risks for skin cancer from excessive sun exposure are well known, the benefits from UV exposure are less well known. Yang and colleagues (1) found an inverse association between measures of sun exposure and overall mortality and mortality from cardiovascular disease. They suggested that one mode of action was through UV and serum vitamin D. There is a large literature developing on the relationship between UV exposure or serum vitamin D and disease. The evidence for an inverse association between serum vitamin D and cancer risk is equivocal and strongest for colorectal cancer (e.g., 14). The association with mortality is also inconsistent, with some cohort studies indicating that high levels of serum vitamin D associated with improved survival (15) and some indicating a need for caution (16). There are many substantiated benefits from attaining optimal vitamin D levels: rickets among the young and bone fractures among the elderly. Optimal levels have yet to be clearly defined. The IOM report found no evidence for maintaining serum vitamin D levels above 30 ng/mL, or 50 nmol/L, which is in direct opposition to many investigators who are promulgating much higher levels (e.g., 17).

Noncancer disease incidence and mortality has also been previously related to higher serum vitamin D levels. As cardiovascular disease-related deaths are anticipated to increase by 80% among females by 2020, this area is important for investigation (18). Among patients with end stage renal disease, 1 alpha-vitamin D and paricalcitol are effective drugs to reduce mortality risk from cardiovascular disease (19–21). Excess parathyroid hormone (associated with low levels of serum vitamin D) increases blood pressure and contributes to cardiovascular disease. Zittermann (19) points out the relatively strong inverse and statistically significant association between ischemic heart disease death rates in Europe and latitude, as a proxy for UV exposure and serum vitamin D levels, 0.49 for females and 0.51 for males.

On the other hand, it is possible that UV exposure may have potential benefits that do not accrue through serum vitamin D. Lucas and Ponsonby (22) concluded that "although the major beneficial effect of UV is as the major source of serum vitamin D, it is not clear that maintaining sun avoidance by supplementing vitamin D will be sufficient to avoid the risks of too little exposure to UV." Increased UV exposure has multiple pathways that serve to protect from disease: endocrine function (23), direct immunosuppression (e.g, 24); immunosuppression due to inhibition of melatonin production (e.g., 25); increased serotonin turnover (e.g., 26); increased alpha melanocyte stimulating hormone (e.g, 27); increased DNA repair capacity (e.g, 28); as well as therapeutic effects on psoriasis (e.g, 29), eczema (e.g, 30), and vitiligo (e.g, 31). Further, evidence for a benefit from UV exposure is relatively strong for autoimmune diseases. Multiple sclerosis (MS) has been shown in ecological studies to have generally greater incidence and prevalence at higher latitudes (32) and analytic studies demonstrate that higher overall UV exposure is inversely associated with MS (e.g., 33). Type I diabetes also shows a latitudinal gradient such that there is a higher incidence at higher latitudes (34).

Sunbeds and increased mortality

The surprising finding that sunbed use is assoicated with increased mortality is not yet explained, and so it may be worth additional speculation. One suspects unmeasured or residual confounding not accounted for by the lifestyle factors controlled in analyses, such as education as a proxy for socioeconomic status. It may, for example, be plausible that there are individuals without the means to take any vacations who use solaria as a substitute for the perceived benefits from sunny holidays abroad. In addition, existing comorbidities may prevent holidays but not solaria use, and these could potentially confound the results. This finding needs replicaton and should support additional study to understand the mechanism for the association found.

Summary

Lack of information on the association between UV radiation and vitamin D or other hormonal and endocrine effects hampers the ability to precisely explain the results of Yang and colleagues (1). However, even with that caveat, these results are likely to add to the weight of the evidence for benefits from sun exposure and risks associated with indoor tanning.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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