Benefits of sun exposure: vitamin D and beyond

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Abstract. Sun exposure has risks and benefits for human health. The best known of these are skin cancer and vitamin D production, respectively. There are a range of other risks and, potentially, benefits, although these are less well-researched. On the benefits side it is difficult to separate out vitamin D and non-vitamin D effects, since exposure of the skin to UV radiation results in both. Oral supplementation with vitamin D will provide only the benefits of vitamin D. The possible benefits of sun exposure beyond vitamin D include immune modulation, control of blood pressure, control of metabolism and weight, and feelings of well-being. The quantitative balance of risks and benefits is not known, but is likely to be variable according to skin type and genetic make-up.

Introduction

Exposure of the skin to UV radiation results in absorption of UV energy by a range of chromophores in the skin: DNA and RNA, 7-dehydrocholestrol (7-DHC, the precursor of vitamin D), pro-opiomelanocortin, trans-urocanic acid, tryptophan and others. This leads to changes in chemical, hormonal and neural signals, with downstream effects on immune cells, the hypothalamic-pituitary-adrenal (HPA) axis, synthesis of vitamin D, DNA damage, release of nitric oxide stores and others. Here we discuss the current state of the evidence on these vitamin D and non-vitamin D pathways whereby sun exposure may have benefits for human health.

Vitamin D

Absorption by 7-DHC of UVB photons causes formation of previtamin D which undergoes a thermal isomerisation to vitamin D. The latter is taken into the blood stream, predominantly bound to vitamin D binding protein. In the liver vitamin D is converted to 25-hydroxyvitamin D (25OHD), which is the metabolite usually measured to determine vitamin D status. The conversion of 25OHD to the active form of the vitamin D, 1,25-dihydroxyvitamin D ($1,25OH_2D$) in the kidney is tightly controlled by parathyroid hormone and feedback loops involving blood calcium levels.

A very large number of adverse health outcomes have been linked to low 25OHD levels in observational studies. In some cases it is not clear if this link represents reverse causality – where having the disease causes the low 25OHD rather than the low 25OHD being a risk factor for the disease. This is particularly a risk in case-control studies, where exposures are compared between those with the disease and those without the disease. It is likely that the cases (with the disease) have been unwell in the weeks preceding participation in the study and blood taking, and thus have low 25OHD levels. Furthermore, there is some evidence that inflammation causes a reduction in 25OHD level (Mangin et al. 2014). However, a number of cohort or nested case-control studies where the 25OHD level is typically taken well before disease onset, also show a link between low 25OHD and increased disease risk. Here it seems unlikely that reverse causality is the explanation (for example, (Munger et al. 2006)).

There are now many randomized trials of vitamin D supplementation. In general, these show little evidence of the marked benefit that expected from the observational studies. There may be a modest benefit for acute upper respiratory infections (Martineau et al. 2017), and for all-cause mortality (Bjelakovic G et al. 2011). The lack of benefit may be because of flaws in the trial design, e.g. not limiting the study to those who are vitamin D deficient, using an insufficient dose of vitamin D, and not being of sufficient length.

An alternative explanation for the discrepancy between observational and intervention studies is that the risks associated with low 25OHD are not linked, or only partly linked to vitamin D *per se*, and largely due to an associated exposure (or lack of exposure). The main determinant of 25OHD levels in many populations (particularly fair-skinned populations) is recent sun exposure (Lucas, R.M. et al. 2013b). The 25OHD level is thus a measure of both sun exposure and vitamin D. Furthermore, a single 25OHD has been shown to be well-correlated with past 25OHD levels over the previous 5-10 years (for blood taken at the same location and same season) (McKibben et al. 2016). We have shown that people largely retain their ranking compared to others for sun exposure over their lifetime (Lucas, R. et al. 2013a). Thus in terms of ranking, a single 25OHD level not only reflects recent sun exposure, but sun exposure over at least the last several years.

Sun exposure

The best evidence for a protective effect of higher levels of sun exposure for human health is probably in relation to the autoimmune disorder, multiple sclerosis (MS). A latitude gradient in the prevalence of MS was first described in the 1920s for the USA and has since been shown for Australia, New Zealand, and globally (Simpson et al. 2011). The incidence and prevalence of MS increase with increasing latitude. Several explanations have been proposed, with increasing vitamin D deficiency with increasing latitude the favoured explanation over many years. Observational studies do support a modest effect of low 25OHD associated with increased risk of MS (Lucas, R.M. et al. 2011,Munger et al. 2006). But the latitude gradient in 25OHD levels is not particularly strong (Lucas, R.M. et al. 2013b), and does not explain the latitude gradient in the incidence of MS (Lucas, R.M. et al. 2011). Furthermore, recent studies show that higher sun exposure over the lifetime is associated with lower risk of MS, and this effect is independent of 25OHD level (Lucas, R.M. et al. 2011). Nevertheless, measures of lifetime sun exposure

could be a proxy for lifetime vitamin D status. An innovative recent multi-ethnic study has shed light on these relationships. The protective effect of higher 25OHD levels was seen in non-Hispanic whites, but not in Hispanics or African Americans. However, the protective effect of higher lifetime sun exposure was seen across all ethnicities (Langer-Gould et al. 2018). The lack of an effect of 25OHD in blacks and Hispanics has been interpreted as a result of the weaker link between sun exposure and 25OHD level in those with darker skin; that is, in whites, but not in Hispanics and African Americans, the 25OHD level reflects recent sun exposure (Figure 1). Of note, vitamin D supplementation studies in people with MS have shown very limited clinical benefit. However a recent trial of UV-B phototherapy in people at high risk of MS, showed a 30% (p=0.06) lower conversion to MS compared to those not receiving phototherapy (with both groups receiving vitamin D supplementation to maintain high 25OHD levels) (Hart et al. submitted).

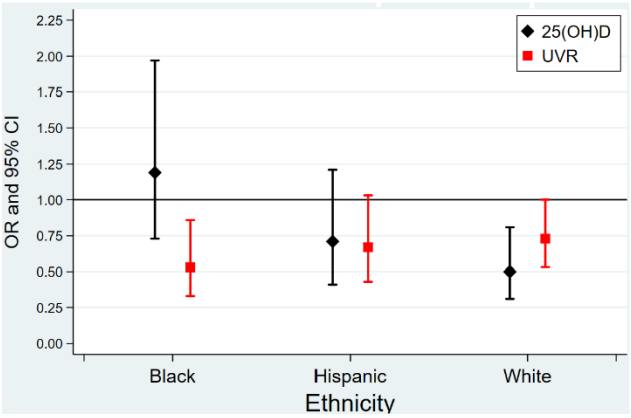

Figure 1. Relationship between serum 25OHD concentration or cumulative UV radiation exposure and odds of multiple sclerosis (based on data from (Langer-Gould et al. 2018)

Other work has shown that UV-A irradiation reduces blood pressure, possibly through release of nitric oxide stores from skin (Liu et al. 2014). Nitric oxide causes arterial vasodilation and UV irradiation also reduces the inflammation that accompanies atherosclerosis.

UV-B phototherapy is used to treat psoriasis and eczema; natural sun exposure probably also has benefits for these conditions that are not commonly considered.

Studies in mice show that low-dose UV irradiation of the skin impairs weight gain in mice fed a high fat diet, and improves glucose tolerance and signs of the metabolic syndrome (Geldenhuys et al. 2014). The pathway is likely to be through release of nitric oxide stores, although UV-induced release of α-melanocyte stimulating hormone (that initiates the tanning response), may have effects on the HPA axis in the central nervous system, to possibly control appetite. Through the same pathway, β-endorphin is produced, inducing feelings of well-being that may contribute to 'addiction' to sun exposure.

Sun exposure is not just UV-B or UV-A, or visible light, but the whole package. Exposure to high intensity blue light outdoors may explain the reduced incidence of myopia seen in studies of a time outdoors intervention. Further, there may be interactive effects between wavebands that are not yet well-understood.

Conclusions

Sun exposure may have considerable benefits for human health beyond vitamin D. Studies that show increased disease risks with 25OHD levels below 50nmol/L may indicate that this level can be used as a guide to the amount of sun exposure required to achieve benefits.

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