Letter to the Editor

European Journal of Cardiovascular Prevention & Rehabilitation

EUROPEAN SOCIETY OF CARDIOLOGY®

European Journal of Cardiovascular Prevention & Rehabilitation
18(4) 678–679

DOI: 10.1177/1741826710389412
ejcpr.sagepub.com

SAGE

Might vitamin D explain the seasonal variation of cardiovascular disease in Tromsø?

Mark R Goldstein[1], Luca Mascitelli[2] and William B Grant[3]

Hopstock and colleagues[1] reported a modest, but significant, increase in incident myocardial infarction in the dark winter months among participants of a large prospective population study (Tromsø Study) in northern Norway. We suggest that the findings are partially related to decreased sunlight exposure and low vitamin D levels during the dark sub-Arctic winter season.

Low blood 25-hydroxyvitamin D (25[OH]D) levels have been found to be associated with increased all-cause mortality, largely fuelled by an increase in cardiovascular disease (CVD) mortality, among non-smokers in the Tromsø population.[2] Vitamin D levels are significantly lower in the winter months in various populations at different latitudes, and there is a definite seasonality of CVD events in both cold and warm climates; CVD events are significantly more common in winter than summer months.[3] Meta-analysis of prospective observational studies on the relation of vitamin D and CVD demonstrate an approximate doubling of CVD mortality in subjects with low vitamin D levels.[4]

Vitamin D is tied to many aspects of atherosclerosis, including blood pressure, plaque stability, inflammation and lipoprotein metabolism. The biologically active form of vitamin D, 1,25-dihydroxyvitamin D, is a negative regulator of the renin-angiotension system.[5] Ultraviolet B (UVB) irradiation increases dermal vitamin D production and has been shown to significantly decrease blood pressure in hypertensive patients.[6] Interestingly, independent of vitamin D, whole-body ultraviolet A (UVA) irradiation has been shown to lower blood pressure in healthy individuals by augmenting the transmigration of nitrite-derived nitric oxide from skin into plasma.[7]

Vitamin D supplementation alters the balance of cytokines by increasing anti-inflammatory interleukin-10 and decreasing pro-inflammatory tumour necrosis factor-α production,[8] which might add stability to atherosclerotic plaque. Moreover, vitamin D insufficiency is associated with increased circulating matrix metalloproteinase-9 (MMP-9) and C-reactive protein (CRP) levels, and MMP-9 and CRP are decreased by vitamin D supplementation,[9] possibly augmenting plaque stability.

In addition, vitamin D levels are positively related to serum insulin growth factor (IGF)-1 levels, up to 25[OH]D blood concentrations of about 32 ng/mL.[10] It is noteworthy that low serum IGF-1 levels have been shown to be related to ischaemic heart disease risk.[11] Recently, vitamin D has been reported to have favourable effects on lipoprotein metabolism. Higher blood 25[OH]D levels are associated with large high-density lipoprotein (HDL) particles, which are more effective in reversing cholesterol transport.[12]

Counterintuitively, the mortality increase in the winter compared to the summer months is more robust at latitudes where the winters are relatively mild.[13] Indeed, the seasonality of CVD events was modest in the cold and dark climate of Tromsø.[1] Perhaps, this paradox might be explained by higher blood melatonin levels of subjects living in areas where the winters are darker and likely colder. Increases in melatonin might lead to decreased CVD through its blood pressure lowering and antioxidant properties and favourable effects on lipoprotein metabolism.[14] Possibly, the beneficial cardiovascular effects of higher blood melatonin during dark winters blunts the negative cardiovascular effects of lower winter blood 25[OH]D levels. It is also plausible that supplementation of vitamin D during the winter months by people living in northern latitudes partially blunts the seasonality of CVD events.[15]

[1]Bonita Springs, FL, USA.
[2]Medical Service, Comando Brigata alpine "Julia", Udine, Italy.
[3]Sunlight, Nutrition, and Health Research Center (SUNARC), San Francisco, CA, USA.

Corresponding author:
Mark R Goldstein, Bonita Springs, FL, USA
Email: markrgoldstein@comcast.net

In conclusion, the lower sunlight exposure and vitamin D status in the Tromsø population during the winter, probably explains the increase in incident myocardial infarction during the winter months.

Disclosure

WBG receives or has received funding from the UV Foundation (McLean, VA), the Sunlight Research Forum (Veldhoven), Bio-Tech-Pharmacal (Fayetteville, AR), and the Vitamin D Council (San Luis Obispo, CA), and the Danish Sunbed Federation.

References

1. Hopstock LA, Wilsgaard T, Njølstad I, Mannsverk J, Mathiesen EB, Løchen M-L, et al. Seasonal variation in incidence of acute myocardial infarction in a sub-Arctic population: the Tromsø Study 1974–2004. *Eur J Cardiovasc Prev Rehabil* 2011; 18: 320–325.
2. Hutchinson MS, Grimnes G, Joakimsen RM, Figenschau Y and Jorde R. Low serum 25-hydroxyvitamin D levels are associated with increased all-cause mortality risk in a general population: the Tromsø study. *Eur J Endocrinol* 2010; 162: 935–942.
3. Zittermann A, Schleithoff SS and Koerfer R. Putting cardiovascular disease and vitamin D insufficiency into perspective. *Br J Nutr* 2005; 94: 483–492.
4. Grandi NC, Breitling LP and Brenner H. Vitamin D and cardiovascular disease: systemic review and meta-analysis of prospective studies. *Prev Med* 2010; 51: 228–233.
5. Li YC, Kong J, Wei M, Chen Z-F, Liu SQ and Cao L-P. 1,25-Dihydroxyvitamin D3 is a negative endocrine regulator of the renin-angiotensin system. *J Clin Invest* 2002; 110: 229–238.
6. Krause R, Bühring M, Hopfenmüller W, Holick MF and Sharma AM. Ultraviolet B and blood pressure. *Lancet* 1998; 352: 709–710.
7. Opländer C, Volkmar CM, Paunel-Görgülü A, van Faassen EE, Heiss C, Kelm M, et al. Whole body UVA irradiation lowers systemic blood pressure by release of nitric oxide from intracutaneous photolabile nitric oxide derivates. *Circ Res* 2009; 105: 1031–1040.
8. Schleithoff SS, Zittermann A, Tenderich G, Berthold HK, Stehle P and Koerfer R. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial. *Am J Clin Nutr* 2006; 83: 754–759.
9. Timms PM, Mannan N, Hitman GA, Noonan K, Mills PG, Syndercombe-Court D, et al. Circulating MMP9, vitamin D and variation in the TIMP-1 response with VDR genotype: mechanisms for inflammatory damage in chronic disorders? *Q J Med* 2002; 95: 787–796.
10. Hyppönen E, Boucher BJ, Berry DJ and Power C. 25-hydroxyvitamin D, IGF-1, and metabolic syndrome at 45 years of age: a cross-sectional study in the 1958 British birth cohort. *Diabetes* 2008; 57: 298–305.
11. Juul A, Scheike T, Davidsen M, Gyllenborg J and Jørgensen T. Low serum insulin-like growth factor 1 is associated with increased risk of ischemic heart disease: a population-based case-control study. *Circulation* 2002; 106: 939–944.
12. Kazlauskaite R, Powell LH, Mandapakala C, Cursio JF, Avery EF and Calvin J. Vitamin D is associated with atheroprotective high-density lipoprotein profile in postmenopausal women. *J Clin Lipidol* 2010; 4: 113–119.
13. Douglas S and Rawles J. Latitude related changes in the amplitude of annual mortality rhythm. The biological equator in man. *Chronobiol Int* 1999; 16: 199–212.
14. Dominguez-Rodriguez A, Abreu-Gonzalez P, Sanchez-Sanchez JJ, Kaski JC and Reiter RJ. Melatonin and circadian biology in human cardiovascular disease. *J Pineal Res* 2010; 49: 14–22.
15. Huotari A and Herzig K-H. Vitamin D and living in northern latitudes – an endemic risk area for vitamin D deficiency. *Int J Circumpolar Health* 2008; 67: 164–178.