Vitamin D and Diabetes

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Abstract. There is current debate around the optimal levels of vitamin D, as measured by serum 25-hydroxyvitamin D (25OHD), required for good health. The current paper reviews two epidemiological studies to determine blood levels of 25OHD associated with lowest risk of diabetes. Findings from a NZ workforce survey and NHANES III in the US show that diabetes risk is lowest in people with 25OHD levels above 80 nmol/L, the same level at which calcium absorption and suppression of parathyroid hormone is maximal. Collectively, these findings suggest that 25OHD levels should be maintained above 80 nmol/L to achieve optimal health.

Introduction

Vitamin D status is determined by blood levels of 25-hydroxyvitamin D (25OHD), the main metabolite of vitamin D (Zittermann, 2003). There is increasing evidence that the diagnostic levels defining vitamin D insufficiency are much higher than the 25OHD level of 50 nmol/L used previously. For example, changes in calcium absorption and blood parathyroid hormone levels occur in people up to 25OHD levels of 80-100 nmol/L (Heaney *et al*, 2003; Kinyamu *et al*, 1998). Evidence from epidemiological studies of vitamin D status and disease risk also can be used to help decide serum 25OHD levels associated with optimal health.

Objective

The purpose of this paper is to review findings from previous epidemiological studies of adult onset (primarily type 2) diabetes to determine blood levels of 25OHD associated with lowest risk of this disease. Two cross-sectional studies of undiagnosed diabetes carried out in New Zealand (Scragg *et al*, 1995) and the United States (Scragg *et al*, 2004) are reviewed.

Background

Evidence exists for a role of vitamin D in type 2 diabetes. *Taq1* receptor polymorphisms are associated with insulin secretion in Bangladeshi in London, who have a high prevalence of type 2 diabetes (Ogunkolade *et al*, 2002), *Bsm1* & *Apa1* polymorphisms are associated with fasting glucose in Caucasians (Ortlepp *et al*, 2003; Oh *et al*, 2002), and receptors to 1,25-dihydroxyvitamin D have been identified in skeletal muscle and liver (Zittermann, 2003), tissues that are involved in insulin resistance.

Methods and Results

Workforce Diabetes Study

The Workforce Diabetes Study was carried out in Auckland and Tokoroa during 1988-1990. Staff at 41 worksites aged 40-64 years (n=5677) were screened, and 80 undiagnosed cases of diabetes and 158 cases of impaired glucose tolerance were detected. These cases were individually matched with controls by sex, age, ethnicity and time of year for measurement of 25-hydroxyvitamin D_3 (Scragg *et al*, 1995). When participants were categorised by tertile of $25OHD_3$, those in the highest tertile ($25OHD_3$ > 82 nmol/L) had about one-third of the odds of diabetes and impaired glucose tolerance (OR=0.36, 95% CI 0.19, 0.71) compared with those in the lowest vitamin D tertile ($25OHD_3$ ≤ 60 nmol/L), after adjusting for confounders (Figure 1).

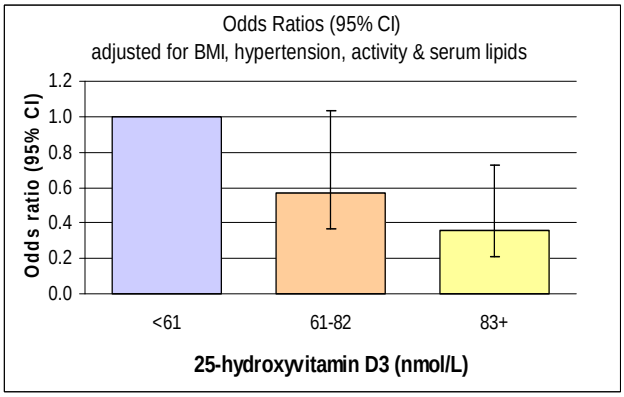

Figure 1. Odds ratios of undiagnosed diabetes and impaired glucose tolerance by tertile of serum $25OHD_3$ in employed NZ men and women.

3rd National Health Nutrition and Examination Survey (NHANES III)

This US study interviewed a representative sample of the US population in 1988-94. Analyses were restricted to 6,228 adults aged >20 years who attended for the morning examination after fasting overnight and provided a blood sample (Scragg *et al*, 2004). An inverse association between serum 25OHD quartile and odds of undiagnosed diabetes was observed in non-Hispanic whites (Figure 2) and Mexican-Americans (data not shown), but not in non-Hispanic blacks. The latter result was surprising, given the low levels of 25OHD in non-Hispanic blacks, and may reflect decreased sensitivity to vitamin D and/or related hormones such as

parathyroid hormone. In comparison with the lowest vitamin D quartile (25OHD ≤43.9 nmol/l), diabetes odds ratios were lowest in the highest vitamin D quartile (25OHD ≥81nmol/L), being 0.25 (95% CI 0.11, 0.60) for non-Hispanic whites (Figure 2) and 0.17 (95% CI 0.08, 0.37) for Mexican-Americans.

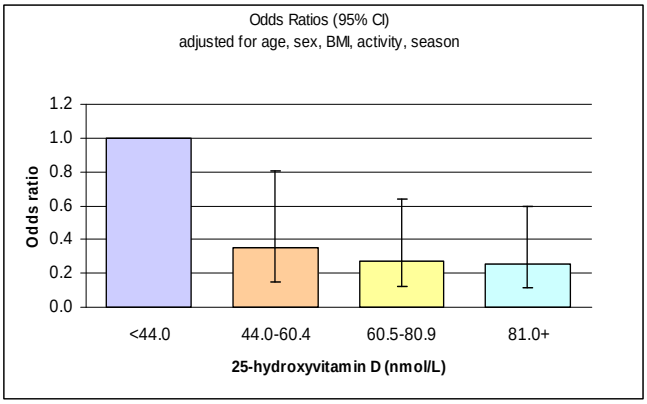

Figure 2. Odds ratios of undiagnosed diabetes by quartile of serum 25OHD in US non-Hispanic whites.

Discussion

The above two studies show inverse associations between vitamin D status and risk of diabetes, with odds ratios progressively decreasing as blood levels of 25OHD increase. The lowest risk of diabetes occurs at 25OHD levels above 80 nmol/L, consistent with the studies showing that calcium absorption and suppression of parathyroid hormone are maximal above these levels (Heaney *et al*, 2003; Kinyamu *et al*, 1998). Collectively, these findings suggest that 25OHD levels should be maintained above 80 nmol/L to achieve optimal health.

Conclusion

This conclusion has implications for public health policy. Recent research indicates that daily intakes of 3000-5000 IU are required to maintain serum 25OHD at 80-100 nmol/L (Vieth, 1999; Heaney *et al*, 2003). Food is only a minor source of vitamin D for the New Zealand population. Supplementation is not a practical strategy to increase vitamin D levels among New Zealanders since high dose vitamin D supplements currently are not available to the general public. The major source of vitamin D is sun exposure. Current policies advising people to minimise sun exposure may need to be revised if future research confirms that vitamin D lowers risk of diabetes and other diseases.

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