COMMENTS AND RESPONSES

Comment on: Davidson et al. High-Dose Vitamin D Supplementation in People With Prediabetes and Hypovitaminosis D. Diabetes Care 2013;36:260–266

NORBERT J. TRIPOLT, PHD[1,2]
MICHAELA EDER[1,2]
TATJANA STOJAKOVIC, MD[3]
STEFAN PILZ, MD, PHD[1]
THOMAS R. PIEBER, MD[1]
HARALD SOURIJ, MD[1,2]

From the [1]Department for Internal Medicine, Division of Endocrinology and Metabolism, Medical University of Graz, Graz, Austria; the [2]Department of Endocrinology and Metabolism, Cardiovascular Diabetology Research Group, Medical University of Graz, Graz, Austria; and the [3]Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Graz, Austria.

Corresponding author: Harald Sourij, ha.sourij@medunigraz.at.

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We have read with interest the work by Davidson et al. (1) reporting in this journal that in a non-Caucasian population with impaired fasting glycemia or impaired glucose tolerance and low vitamin D levels, vitamin D supplementation had no effect on estimates of insulin secretion, insulin sensitivity, or incident diabetes.

Our research group started a similar study (ClinicalTrials.gov number, NCT01183442) in Caucasians with postchallenge hyperglycemia (i.e., 2-h glucose ≥140 mg/dL), vitamin D deficiency, and coronary artery disease. As in the study by Davidson et al. (1) we had to prescreen a high number of patients (n = 1,814). Five hundred seventy-nine were potentially eligible, of which only 178 were willing to undergo an oral glucose tolerance test and to participate in this 12-month study. Fifty-three (30%) had postchallenge hyperglycemia, and out of these only 42% had hypovitaminosis D. Finally, only 22 patients were randomized and the trial committee decided to stop the trial prematurely due to unfeasibility to recruit the intended number of 140 subjects.

Previous large-scale outcome trials in patients with impaired glucose tolerance have already demonstrated the need for screening large numbers of subjects to finally enroll the required number of participants. In the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) trial 21.9% of the 43,502 subjects screened were finally randomized (2) while the Study To Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial randomized 9.6% of the 14,742 subjects screened (3).

If studies require vitamin D insufficiency as an additional inclusion criterion, recruitment becomes even more difficult. One reason could be that low vitamin D levels might represent a marker of reduced health status, and these subjects might be less likely to participate in intervention trials. In addition, because of the increasing number of epidemiological publications, suggesting a beneficial association of vitamin D with several health outcomes, the number of patients with vitamin D supplementation is steadily increasing.

Interestingly, currently 19 intervention trials investigating the impact of vitamin D supplementation on various outcome measures in subjects with impaired glucose tolerance or prediabetes are registered on www.clinicaltrials.gov. However, results have been published for only 2 of these mainly short-term studies, although half of the trials commenced at least 3 years ago.

Although subjects with postchallenge hyperglycemia seem to be an interesting target cohort to study the effect of vitamin D supplementation on glucose metabolism, investigators need to keep in mind that recruitment is challenging and that the number of patients needed to screen will likely be more than 10- to 15-fold higher than the number of patients finally enrolled when designing this kind of study.

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