

Vitamin D status and progression to diabetes in patients at risk for diabetes: an ancillary analysis in the Diabetes Prevention Program randomized controlled trial

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The objective of the study was to investigate the longitudinal association between vitamin D status and risk of incident diabetes in the Diabetes Prevention Program (DPP), a 3-arm trial comparing intensive lifestyle modification or metformin vs. placebo for prevention of diabetes in patients with pre-diabetes.

Over a mean 3.2-year follow-up period, in discrete-time proportional hazards models, we assessed the association between plasma 25OHD, measured at yearly intervals, and incident diabetes in the cohort of 2,039 participants randomized to either intensive lifestyle (n=1,017) or placebo (n=1,022). Analyses were adjusted for age, gender, BMI, race, UV index, family history of diabetes, hypertension, smoking, alcohol consumption, C-reactive protein, kidney function, physical activity and intervention. Variables measured at multiple study time points (25OHD, BMI and physical activity) entered the analyses as time-varying "lagged" covariates, as the mean of the previous and current visit at which diabetes status was assessed.

After multivariate adjustment, participants in the highest tertile of 25OHD (median 25OHD 30.1 ng/mL) had a hazard ratio of 0.74 (95%CI, 0.59 to 0.93) for developing diabetes compared to participants in the lowest tertile (median 25OHD 12.8 ng/mL). When analyses were repeated by categories of 25OHD based on cut-points suggested by the 2010 Institute of Medicine Dietary Reference Intake report on calcium and vitamin D, there appeared to be a 'dose-effect' with the hazard ratio for incident diabetes being lowest (0.46; 95%CI, 0.23 to 0.90) in the highest category (25OHD \geq 50 ng/mL) compared to the lowest category (25OHD <12 ng/mL) with no evidence of a threshold. In subgroup analyses by tertiles, the association was in the same direction in placebo (0.72; 95%CI 0.53, 0.96) vs. lifestyle arm (0.80; 95%CI 0.54, 1.14) (p=0.67 for interaction).

Higher vitamin D status, assessed repeatedly during the follow-up period, is associated with lower risk of diabetes among persons at high risk for diabetes, even after adjusting for lifestyle interventions (dietary changes and increased physical activity) known to decrease diabetes risk. The role of vitamin D in reducing diabetes risk needs to be confirmed in vitamin D supplementation trials.