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Randomized Controlled Trial for the Effect of Vitamin D Supplementation on Vascular Stiffness in CKD

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Abstract

Background and objectives Vitamin D is implicated in vascular health in CKD. This study compared placebo, calcifediol, and calcitriol treatment with changes in vascular stiffness, BP, proteinuria, mineral metabolism parameters, C-reactive protein, and fibroblast growth factor 23 in patients with stable CKD.

Design, setting, participants, & measurements We conducted a double-blind, randomized controlled trial in out-patient CKD clinics in Vancouver, Canada, from February of 2011 to August of 2014, enrolling 119 patients with an eGFR of 15–45 ml/min per 1.73 m^2. Change in pulse wave velocity (PWV) was measured after 6 months of treatment with a fixed dose of oral calcifediol (5000 IU 25-hydroxyvitamin D_3), calcitriol (0.5 μg 1,25-dihydroxyvitamin D_3), or placebo, thrice weekly.

Results Eighty-seven participants were evaluated. Mean age was 66 years, 71% were men, 40% were diabetic, and mean baseline PWV was 11.5 m/s (SD=3.9 m/s). After 6 months, the PWV decreased in the calcifediol group (mean change, −1.1; 95% confidence interval [95% CI], −2.2 to 0.1 m/s), remained unchanged in the calcitriol group (mean change, 0.2; 95% CI, −0.9 to 1.4 m/s), and increased in the placebo group (mean change, 1.1; 95% CI, −0.1 to 2.2 m/s). The overall *P* value for between-arm changes was 0.03. Absolute PWV change was significantly different between groups ($P=0.04$): the combined vitamin D treatment group saw decreased PWV (mean change, −0.4; 95% CI, −1.2 to 0.4 m/s) whereas the placebo group saw increased PWV (mean change, +1.1; 95% CI, −0.1 to 2.2 m/s). The treatment group demonstrated significantly decreased serum parathyroid hormone (mean difference, −0.5; 95% CI, −0.7 to −0.3 ln[pg/ml]; $P<0.001$) and increased calcium (mean difference, 0.4; 95% CI, −0.1 to 0.7 mg/dl; $P=0.02$). In observational analysis, participants in the highest 25-hydroxyvitamin D tertile at trial end had significant decreases in PWV (mean change, −1.0; 95% CI, −2.0 to 0.0 m/s) compared with the middle and lowest tertiles ($P<0.01$). Side effects were minor and rare.

Conclusions Six months of supplemental vitamin D analogs at fixed doses may achieve a reduction of PWV in patients with advanced CKD. Because the treatment effect was attenuated when baseline PWV was included as a covariate, these findings should be replicated in larger populations and further studied.

Vitamin D | vascular calcification | vascular disease | mineral metabolism | Aged | Arm | blood pressure | C-Reactive Protein | Calcifediol | Calcitriol | calcium | Canada | diabetes mellitus | Fibroblast Growth Factors | Humans | Male | Minerals | Outpatients | parathyroid hormone | proteinuria | Pulse Wave Analysis | Renal Insufficiency, Chronic | Vascular Stiffness | Vitamins | fibroblast growth factor 23

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