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Research Article

Hypovitaminosis D predicts the onset of orthostatic hypotension in older adults

Nicola Veronese, MD[a,*], Caterina Trevisan, MD[a], Francesco Bolzetta, MD[a], Marina De Rui, MD[a], Sabina Zambon, MD[b,c], Estella Musacchio, ScD[c], Leonardo Sartori, MD[c], Brendon Stubbs, PhD[d,e], Egle Perissinotto, ScD[f], Gaetano Crepaldi, MD[b], Enzo Manzato, MD[a,b], and Giuseppe Sergi, MD[a]

[a]*Department of Medicine (DIMED), Geriatrics Division, University of Padova, Padova, Italy;*
[b]*National Research Council, Neuroscience Institute, Padova, Italy;*
[c]*Department of Medicine DIMED, Clinica Medica I, University of Padova, Padova, Italy;*
[d]*Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, United Kingdom;*
[e]*Health Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom; and*
[f]*Department of Cardiac, Thoracic and Vascular Sciences—Biostatistics, Epidemiology and Public Health Unit, University of Padova, Padova, Italy*

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Abstract

A number of small cross sectional studies have demonstrated that hypovitaminosis D (represented by low 25 hydroxyvitamin D (25OHD) levels) is associated with orthostatic hypotension (OH). We investigated if hypovitaminosis D is associated with the onset of OH in older adults over a follow-up of 4.4 years. 25OHD was categorized using sex-specific quartiles; OH was defined as a drop of $\leq$20 mm Hg in systolic or $\leq$10 mm Hg in diastolic blood pressure $<$3 minutes of standing. Among 1308 elderly without OH at baseline, using an adjusted logistic regression analysis and taking those with higher baseline serum 25OHD as reference, there was a significant increase in the onset of OH in those with lower serum 25OHD levels. The association was significant only in women when we stratified by sex. In conclusion, hypovitaminosis D predicts the onset of OH in older adults, particularly in women. J Am Soc Hypertens 2016;10(9):724–732.

Keywords: Aged; orthostatic hypotension; vitamin D.

Introduction

Orthostatic hypotension (OH) is a common condition in the elderly. Its prevalence significantly varies with age reaching approximately 30% in those aged $\geq$70 years.[1] OH is traditionally related to a greater risk of falls, traumas, and fractures.[1] However, recent research has proposed OH as a potential cardiovascular risk factor because OH seems to be able to predict cardiovascular events and all-cause mortality.[2–5]

A number of studies have demonstrated a possible role for hypovitaminosis D defined as lower serum 25-hydroxyvitamin D (25OHD) levels, as a potential risk factor for vascular diseases, including hypertension. The association between 25OHD and hypertension was recently reported in a large meta-analysis, showing that increased 25OHD concentrations were significantly associated with

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Conflict of interest: none.

*Corresponding author: Nicola Veronese, MD, University of Padova, Department of Medicine - DIMED, Geriatrics Division, Via Giustiniani 2, Padova 35128, Italy. Tel: +390498218492; Fax: +390498211218.

E-mail addresses: ilmannato@tiscali.it, ilmannato@gmail.com

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decreased odds of hypertension.[6] Vitamin D receptors are present in endothelial cells and may have a crucial role in the modulation of vessels in animal models.[7] Therefore, it appears possible that vitamin D could play a role in modulating vascular response during orthostatism.

However, data about the role of hypovitaminosis D as a possible risk factor for OH in humans are predominantly limited to cross-sectional studies.[8–13] Altogether, these studies showed a significant association between hypovitaminosis D and OH,[8–11] although the number and type of adjustments seem to be an important factor.[12] To the best of our knowledge, only one study has prospectively assessed the association between hypovitaminosis D and OH.[14] The authors found that hypovitaminosis D predicts the onset of OH at follow-up but had various limitations, in particular the small sample size (n = 51) and the short follow-up (1 year) which limits the conclusions of these findings.[14]

We therefore aimed to investigate the association between hypovitaminosis D and the onset of OH in a large representative cohort of older men and women over a mean follow-up of 4.4 years. We hypothesized that low-serum 25OHD would predict the onset of OH at the follow-up.

Methods

Data Source and Subjects

This work is based on data of the *Progetto Veneto Anziani* (Pro.V.A.) study, an observational cohort study of all community-dwelling subjects aged ≥65 years residing in Camposampiero and Rovigo (two towns in northern Italy surrounded by rural and industrial areas) without using any specific exclusion criteria.[15] The baseline visit was made between October 1995 and November 1997.

The follow-up evaluation was scheduled to occur at 4 years after baseline. The follow-up period was in mean 4.4, censoring the data after 6 years from baseline evaluation.

The local ethical committees of Padova University and the Local Health Units (USSL) n. 15 and n. 18 of the Veneto Region approved the study protocol, and participants gave their written informed consent.

Clinical Data

Participants were examined at city hospitals by trained physicians and nurses. Regular physical activity was defined as ≥4 h/week (ie, the upper half of the median split of the entire sample) in the previous month of at least moderate physical activity (brisk walking, cycling, gardening, dancing, or physical exercise). Smoking status was classified as ‘‘current’’ versus ‘‘former (for at least 1 year in the past)/never’’. Heavy alcohol drinkers were defined using the criteria suggested by the National Institute of Alcohol Abuse and Alcoholism, that is, more than 15 drinks weekly for men and 8 for women.[16] Living alone was categorized as ‘‘yes’’ versus ‘‘no’’.

We collected the following anthropometric parameters: height (measured or estimated from knee-height, when this proxy indicator was more accurate), weight, body mass index (in kg/m^2).

Functional status and social independence were assessed using the activities of daily living and instrumental activities of daily living (IADL).[17,18] Cognitive function was assessed using 30 items mini-mental state examination.[19]

Participants' clinical status and comorbidities were evaluated by board-certified physicians through standardized questionnaires considering anamnestic data, self-reported symptoms, medical and hospital records, and results from blood tests and physical examination. For the purpose of our study, the following diseases were assessed: history of hypoacusis, hypovisus, diabetes mellitus, cardiovascular diseases (CVDs), hip fracture and osteoarthritis, and hypertension.[15] Diabetes was defined as fasting plasma glucose levels ≥7.0 nmol/L, HbA1c ≥ 6.5%, the use of glucose-lowering drugs, or a history of a 2-hour post-load glucose ≥11.1 mmol/L.[20] As CVD, we considered the presence of one of the following: congestive heart failure; angina requiring a stent, angioplasty or hospitalization; myocardial infarction; and stroke. Hypertension was defined as the presence of systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or current use of antihypertensive medications.[21] Both at the baseline and at the follow-up, the physician performing the physical examination diagnosed any disease using all the previously listed measures. A specialist in the field (eg, a cardiologist for CVD) confirmed any disease presence using a standardized algorithm considering all the medical information collected on each participant.

Laboratory Tests

A venous blood sample was obtained after an overnight fast for biochemical tests, which were performed at the central laboratory of Padova hospital using standard and quality-controlled procedures. Renal function was assessed using the estimated glomerular filtration rate with the Modified Diet in Renal Disease formula. Serum intact parathormone (PTH) levels were measured using a 2-site immunoradiometric assay (N-tact PTHSP; DiaSorin): the intraassay and interassay coefficients of variation (CVs) for parathormone were 3.0% and 5.5%, respectively. Season of blood collection was defined as winter, spring, summer, or autumn.

Definition of Risk Categories

Serum 25OHD levels were measured by radioimmunoassay (RIA kit; DiaSorin). The intra-assay and interassay