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Serum vitamin D and functional impairment in octogenarian women

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ABSTRACT

Purpose: Serum vitamin D deficiency has been associated with frailty in people aged 65 and over, however its relationship with functional impairment has not been investigated in octogenerian (aged 80–90 years) institutionalized women.
Methods: We assessed functional impairment in this latter group by measuring frailty syndrome and other geriatric and psychological assessment scales: the Tinetti gait and balance index to determine the risk for falls, the Barthel index to measure the basic activities of daily living, the Lawton index for instrumental activities, the mini-mental score examination test for cognitive impairment, the Yesavage scale for geriatric depression, and the Norton scale for the risk of ulceration.
Results: Frail individuals had significantly reduced serum vitamin D concentrations (measured as total 25-hydroxyvitamin D; 25(OH)D) compared to robust individuals, but reduced 25(OH)D concentration did not significantly correlate with frailty syndrome severity, and mean 25(OH)D concentrations were within the recommended levels in all groups. The 25(OH)D concentration did not correlate with any of the blood analytical parameters measured and with the geriatric assessment scales used, suggesting a selective relationship with frailty.
Conclusion: These results highlight the need to individualize treatment such as vitamin D supplementation in order to treat frailty syndrome.

1. Introduction

Frailty syndrome is characterized by decreased physical functioning and a higher risk for poor outcomes such as an increased incidence of falls, fractures, disability, and comorbidity, increased health care expenditure, and premature mortality (Fried et al., 2001; Fugate-Woods et al., 2005). The concept of frailty has grown in importance because its prevention or hindrance delays the onset of disabilities and dependence (Fried et al., 2001). Frailty syndrome is primarily defined using a standardized phenotype based on five physical criteria as first described by Fried et al. in their Cardiovascular Health Study (Fried et al., 2001), although several other scales for measuring frailty have also been proposed (Fernández-Garrido, Ruiz-Ros, Buigues, Navarro-Martinez, & Cauli, 2014). Frailty has been associated with changes in several physiologic systems, coagulation, hematologic, endocrine systems, micronutrients-vitamins and a low-chronic inflammatory state (Walston et al., 2002). Importantly, a decreased vitamin D concentration in blood has been repeatedly linked to frailty syndrome (Fernández-Garrido et al., 2014; Morley et al., 2013; Smit et al., 2012; Wilhelm-Leen, Hall, Deboer, & Chertow, 2010). An adequate concentration of this vitamin is required to maintain sufficient blood calcium and phosphorous levels to maintain strong bones, regulate cell growth and differentiation, modulate immune system activity, influence muscle metabolism, and regulate some cerebral processes (Adams & Hewison, 2010; Asamura et al., 2010). However, one recent clinical trials have found that vitamin D supplementation does not have any beneficial effects on frailty syndrome (Latham et al., 2003). Moreover daily administration of high vitamin D3 doses (50,000 IU) did not improve physical performance for patients with heart failure despite an increase in their serum 25(OH)D concentration (Boxer et al., 2013). These results suggest that under some circumstances the strength of the association between vitamin D and frailty can be weak or absent.

Most of the studies showing a link between blood vitamin D concentrations and frailty analyze the relationship in samples of community-dwelling individuals with a wide range of ages (generally aged 65 years or more) but exclude older institutionalized adults. In addition a large epidemiological study conducted in Italy demonstrated that vitamin D insufficiency was significantly associated with frailty only in men (Shardell et al., 2009). To our knowledge, the relationship between

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vitamin D, frailty, and other geriatric assessment measurements in old (aged 75 years or more) institutionalized women have not been investigated.

Our three main objectives in this work were:

(1) To evaluate the vitamin D concentration, measured as 25(OH)D, in blood in relation to the severity of frailty syndrome in older, non-osteoporotic, institutionalized women.
(2) To assess the relationship between vitamin D and geriatric assessment tool measurements (the Tinetti scale for gait and balance, the mini-mental score examination [MMSE] test for cognitive function, the Barthel index for the basic activities of daily life, the Norton scale for the risk of pressure ulcers, the Yesavage scale for geriatric depression, and the Lawton index for instrumental activities of daily life).
(3) To evaluate the relationship between vitamin D and other analytical parameters (erythrocyte and platelet count, hemoglobin, hematocrit, glucose, urea, uric acid, cholesterol, triglyceride, creatinine, glutamic oxaloacetic transaminase [GOT], and glutamic pyruvic transaminase [GPT] concentration).

2. Materials and methods

2.1. Study population

This was a clinical study with a cross-sectional design performed on institutionalized elderly women living in one of four nursing homes (*GeroResidencias La Saleta*, Valencia). The inclusion criteria were: institutionalized for at least 6 months, ability to rise from a chair and walk six meters, and aged 65 years or older. The exclusion criteria were: severe cognitive impairment (MMSE score less than 21), severe psychiatric disease or blindness, acute infections or known cancer, primary hyperparathyroidism, or vitamin D and/or calcium supplementation. The research was undertaken in compliance with the requirements of the Declaration of Helsinki and the entire study protocol was approved by the local ethical committee at the University of Valencia (reference number: H1384175284261). All participants gave written informed consent before being enrolled in the study.

2.2. Variables

The variables included socio-demographic characteristics (age, body mass index, and smoking), and measurement of the five frailty criteria (involuntary weight loss, low energy or exhaustion, slow mobility, muscle weakness, and low physical activity) according to Fried et al. (2001) as described in the next section. Geriatric assessment was achieved by evaluating participants with the Tinetti scale (for gait and balance), the MMSE Test (for cognitive function), the Barthel index (for basic activities of daily life), the Norton scale (for the risk of pressure ulcers), the Yesavage scale for geriatric depression, and the Lawton index (for instrumental activities of daily life).

2.3. Measurement of frailty criteria

Frailty was measured by assessing the presence or absence of the five characteristics of the Fried criteria (Fried et al., 2001), which were defined and evaluated as follows:

1) Weight loss, defined as the unintentional loss of 4.5 kg or more in the past year.
2) The exhaustion criterion was considered present if the participant answered “Often” or “Most of the time” to the question “How often in the last week did you feel that everything you did was an effort?” included in the Center for Epidemiologic Studies-Depression scale (Asamura et al., 2010; Orme, Reis, & Herz, 1985; Radloff, 1977).
3) Physical inactivity: defined as participants who performed no physical activity, spent most of the time sitting, and rarely took a short walk or performed any other non-demanding physical activity. Low physical activity was quantified using the Spanish adaptation for women of the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ; Bischoff-Ferrari, Giovannucci, Willett, Dietrich, & Dawson-Hughes, 2006; Elosua, Marrugat, Molina, Pons, & Pujol, 1994; Elosua et al., 2000; Holick, 2004; Thomas et al., 1998; Ruiz-Comellas et al., 2012). The MLTPAQ is administered by a trained interviewer who is provided with detailed instructions and a list of very clearly defined physical activities (PAs). Total energy expenditure from leisure time PA (EEPAtotal) can be obtained with this questionnaire and was used to quantify PA (Jacobs, Ainsworth, & Hartman, 1993; Lips, 2001). Participants were given a list of suggested activities and asked to mark those performed in the last year. To avoid memory bias, as far as possible, the activities performed during the last week were collected first, followed by those performed the last month, the last quarter, and finally the last year, always including the former periods. For validation purposes, only information referring to the last year was used.
4) Slow walking speed, based on the 4,6 walk gait speed test, was defined when the participant corresponded to the worst quintile for the group, after adjustment for sex and height according to the standards of the Short Physical Performance Battery (Guralnik et al., 1994; Shardell et al., 2009).
5) To assess weakness hand grip strength was measured with a Jaymar hand-held hydraulic dynamometer as an approximation of general muscle strength, and assessed according to the standards of the Hispanic Established Populations for the Epidemiologic Studies of the Elderly (Dawson-Hughes et al., 2005; Ottenbacher et al., 2002).

2.4. Vitamin D measurement

25(OH)D (the sum of both 25(OH)D2 and 25(OH)D3, derived from ergocalciferol and cholecalciferol respectively) was measured in serum samples by gas chromatography. First a solid-phase extraction (SPE) was applied to serum samples according to a previously devised protocol (George & Szczesniewski, 2009). The elutes were evaporated and the residue was derivatized using a mixture of N,O-bis(trimethylsilyl) trifluoroacetamide (BSTFA)/pyridine, then resuspended and dissolved in 60 μL of BSTFA with 1% trimethylchlorosilane (TMCS), and injected into the GC/MS instrument for analysis (Cauli, Mansouri, Agusti, & Felipo, 2009).

2.5. Measurement of hematological and biochemical markers

Fasting blood samples were collected in the morning. The hemoglobin concentration, and white blood cell, erythrocyte, and platelet counts were measured on automated instruments at local hematology laboratories near the nursing homes. Biochemical serum analyses included glucose, urea, urate, cholesterol, triglycerides, creatinine, GOT, and GPT. All samples were kept at 4–6 °C and processed within 2 hours of the blood collection. Blood serum (5 ml) was obtained by collecting blood in BD Vacutainer tubes and centrifuging them at 500 g for 10 min at room temperature.

2.6. Statistical analysis

Descriptive statistics, including a measurement of central tendency (mean), standard error of the mean (SEM), and range values were used to describe all the quantitative variables. The normal distribution of each variable was estimated with the Kolmogorov–Smirnov test. Given that none of the variables were normally distributed, correlation was analyzed using the Spearman correlation coefficient. Linear regression analysis was used to specify the association between changes in vitamin D (measured as 25(OH)D) and any variables that were significant in the previous analysis. The non-parametric Kruskal–Wallis test was performed to verify any possible differences between groups. Statistical