Hypovitaminosis D in African Americans Residing in Memphis, Tennessee With and Without Heart Failure

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ABSTRACT: *Background*: Factors contributing to heart failure (HF) in African Americans (AA) are under investigation. Reduced 25(OH)D confers increased cardiovascular risk, including HF. *Methods*: We monitored serum 25(OH)D, $1,25(OH)_2D_3$, parathyroid hormone (PTH), and creatinine clearance in 102 AA residing in Memphis: 58 hospitalized with decompensated HF of ≥4 weeks in 34 (21 men; 53.3 ± 1.8 years) or of 1 to 2 weeks in 24 (17 men; 49.6 ± 2.4 years) and associated with a dilated cardiomyopathy and reduced ejection fraction (<35%); 19 outpatients with compensated HF (14 men; 52.6 ± 2.7 years) with comparable ejection fraction; 16 outpatients (9 men; 55.4 ± 2.9 years) with heart disease, but without HF; and 9 healthy volunteers (3 men; 35.8 ± 3.5 years). *Results*: Serum 25(OH)D ≤30 ng/mL was found in 96% and 90% with protracted or short-term decompensated HF, where it was of moderate to marked severity (<20 ng/mL) in 83% and 76%, respectively. In patients with either compensated or no HF, 25(OH)D <30 ng/mL was found in 95% and 100%, respectively, and in 30% of volunteers. Normal serum $1,25(OH)_2D_3$ did not differ between patients. Serum PTH >65 pg/mL was found in all AA with decompensated HF of ≥4 weeks (132.4 ± 12.0 pg/mL) and 67% with 1 to 2 weeks duration (82.3 ± 7.9 pg/mL), but only 11% with compensated HF (45.8 ± 6.1 pg/mL), 12% without HF (29.6 ± 5.4 pg/mL), and none of the volunteers (31.1 ± 3.9 pg/mL). Creatinine clearance did not differ between patient groups. *Conclusions*: Hypovitaminosis D is prevalent amongst AA residing in Memphis, with or without HF. Elevations in serum PTH in keeping with secondary hyperparathyroidism are only found in AA with decompensated HF, where hypovitaminosis D and other factors are contributory. **KEY INDEXING TERMS:** Hypovitaminosis D; Secondary hyperparathyroidism; Heart failure; African Americans. **[Am J Med Sci 2008;335(4):292–297.]**

Heart failure (HF) is a major health problem. Amongst African Americans (AA), HF is thought to be more prevalent, occurring at an earlier age with greater severity in its presentation, and follows a more progressive downhill clinical course.[1–4] Multiple factors, including longstanding hypertension, renal dysfunction, and diet have been implicated in the greater propensity for HF in AA.[4–7] In the United States, reduced serum 25(OH)D levels in adults are associated with cardiovascular disease risk factors.[8,9]

Worldwide, vitamin D insufficiency is prevalent in adults living in an urban environment with reduced direct sunlight exposure; dietary sources alone do not provide adequate amounts of vitamin D to correct it.[10,11] Hypovitaminosis D may be particularly prevalent in dark-skinned, urban-dwelling individuals.[12] Melanin is a natural sunscreen that requires longer periods of exposure to the ultraviolet B (280–315 nm) component of sunlight for the skin to convert inactive vitamin D to sufficient quantities of vitamin D_3.[13]

Vitamin D deficiency may adversely affect cardiac structure and function.[14,15] It has been associated with congestive heart failure (CHF).[16] Marked reductions in serum 25(OH)D levels (<10 ng/mL) were found in a small number of Caucasian adults with advanced HF residing in the northeastern United States (latitude 42°N) and <15 ng/mL in patients with HF living in western Europe (latitude 52°N).[16,17] In South East England, a dilated reversible cardiomyopathy that can be fatal is seen in dark-skinned, exclusively breastfed

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infants, especially toward the end of winter.[18] In an earlier study, conducted here in Memphis (latitude 35°N) during the summer of 2005, we found reduced 25(OH)D levels (<30 ng/mL) in a majority of 25 AA with a dilated cardiomyopathy and reduced ejection fraction (EF <35%).[19] Values in excess of 30 ng/mL are needed to maximize intestinal calcium absorption and to minimize elevations in parathyroid hormone (PTH) and disturbances in calcium homeostasis.[20]

Since reporting our preliminary findings, we monitored 25(OH)D, a marker of vitamin D stores generated by the 25-hydroxylation of vitamin D_3 in the liver, and serum $1,25(OH)_2D_3$ (or calcitriol), a biologically active steroid hormone produced by the kidneys that contributes to the regulation of PTH, in 102 AA residing in Memphis, an urban location, throughout its 4 seasons. This included: patients with HF having EF <35% due to a dilated (idiopathic) or ischemic cardiomyopathy and who were hospitalized because of their decompensated HF, despite medical management; compensated outpatients with comparable EF; outpatients with heart disease without HF; and healthy volunteers. We also monitored serum PTH, given that hypovitaminosis D can lead to secondary hyperparathyroidism (SHPT), and serum creatinine with calculated creatinine clearance (CrCl) to address renal function.

Methods

Study Population

This study, approved by the institutional review board of the University of Tennessee Health Science Center, consisted of 102 AA (59 men, 43 women; 51.1 ± 1.2 years, 24–79) who were divided into: 77 patients with a failing heart, defined by echocardiographic EF of <35%; 16 outpatients without HF; and 9 healthy volunteers. Individuals were enrolled equally during the 4 seasons in Memphis.

Heart Failure. Of the 77 patients with HF, 58 were hospitalized at the Regional Medical Center here in Memphis because of their symptomatic status (NYHA Class III and IV) and were considered to have decompensated HF. This included 38 men and 20 women with a mean age of 51.9 ± 1.6 (27–79). In 34 of these patients (21 men, 13 women; 53.3 ± 1.8 years, 33–79), the duration of their symptomatic HF was protracted (≥4 weeks) whereas in 24 patients (17 men, 7 women; 49.6 ± 2.4 years, 27–73) their symptomatic failure was of shorter duration (1–2 weeks). We divided the patients with decompensated failure into those with protracted versus shorter durations to their symptomatic failure given that secondary aldosteronism, which contributes to salt and water retention and associated symptoms, is accompanied by heightened excretion of calcium and magnesium in both urine and stool.[21] The longer the duration of the salt-avid state, the greater the excretory losses of these divalent cations and thereby, we reasoned, an increased propensity for ionized hypocalcemia and hypomagnesemia with SHPT.[19] There were 19 ambulatory outpatients (14 men, 5 women; 52.6 ± 2.7 years, 36–75) with comparable reduction in EF, who were followed here in the Cardiology Continuity Clinic and were considered to have minimally symptomatic, compensated failure (NYHA Class I and II).

HF was due to an idiopathic (dilated) cardiomyopathy in 67 patients or an ischemic cardiomyopathy in 10. At the time of admission, patients were being treated with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker, furosemide, and spironolactone while 17 were medically untreated with newly diagnosed CHF. The dosage of these agents did not differ between those with either protracted or short-term decompensated failure. Ambulatory patients with compensated HF were comparably treated.

Heart Disease, Nonheart Failure. Sixteen outpatients (9 men, 7 women; 55.4 ± 2.9 years, 28–74) were followed in the clinic for the evaluation and management of conditions other than HF (eg, palpitations, syncope, chest pain, arrhythmia, or hypertension). This group was considered to represent nonheart failure controls.

Volunteers. Nine AA volunteers (3 men, 6 women; 35.8 ± 3.5 years, 24–58) without known cardiovascular or other illnesses were included in this study and served as healthy controls.

Exclusion Criteria. None of the patients were receiving insulin, estrogen, a glucocorticoid, growth hormone, or thyroxine. None had disorders affecting bone metabolism, including rheumatoid arthritis, Paget's disease, osteomalacia, primary hyperparathyroidism, hyperthyroidism, osteogenesis imperfecta, gastric resection, inflammatory bowel disease, or a history of fragility fractures. And none of the patients had disorders that could lead to reduced ionized $[Ca^{2+}]_o$ or $[Mg^{2+}]_o$ including sepsis, pancreatitis, blood transfusion, surgery, chronic alcoholism, or metabolic alkalosis.

Serum 25(OH)D, 1,25(OH)$_2$D$_3$, and PTH

Blood for determination of 25(OH)D, $1,25(OH)_2D_3$, and PTH was obtained in the morning during the first 48 hours of admission, while in outpatients it was obtained during the afternoon of their clinic visit.

Creatinine Clearance

CrCl was calculated by the Cockroft–Gault formula using serum creatinine obtained at the time of hospital admission or as an outpatient.[22]

Statistical Analysis

Values are presented as mean ± SEM. Data were analyzed by Mann-Whitney rank sum test using SigmaStat statistical software (version 2.0; Systat Software, Inc., Point Richmond, CA). Significant differences between individual means were assigned when P values were <0.05.

Results

Serum 25(OH)D

We graded the severity of hypovitaminosis D as mild, moderate, and severe based on serum 25(OH)D levels of 20 to 30, 10 to 19, and <10 ng/mL, respectively. As seen in Figure 1, all but one of the AA patients (96%) with protracted decompensated HF of 4 weeks or more had a serum 25(OH)D of ≤30 ng/mL (13.9 ± 1.3; 7 to 31 ng/mL); it was of marked severity (<10 ng/mL) in 29% and moderate to marked severity (<20 ng/mL) in 83%. In patients with decompensated failure of a shorter duration (1–2 weeks), serum 25(OH)D levels (15.1 ± 2.6; 7 to 54 ng/mL) were ≤30 ng/mL in all but 2 patients (90%), and was of marked severity in 62% and moderate to marked severity in 76%. In the 19 AA outpatients with compensated HF, serum 25(OH)D levels (16.9 ± 2.2; 7 to 43 ng/mL) were found to be ≤30 ng/mL in 95%, including 32% in whom it was <10 ng/mL and 74% with moderate to marked severity. Reduced 25(OH)D levels in keeping with hy-