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Relation of oral 1α-hydroxy vitamin D₃ to the progression of aortic arch calcification in hemodialysis patients

Abstract The role of decreased active vitamin D levels on vascular calcification has not been elucidated in hemodialysis (HD) patients. The aim of the present study was to evaluate the relationship between progression of aortic arch calcification (AoAC) and prescribed dose of 1α-hydroxy vitamin D. The enrolled study subjects were 65 (40 men and 25 women) HD patients. Calcification of the aortic arch was semiquantitatively estimated with a score (AoACS) on plain chest radiology. Change in AoACS (ΔAoACS) was obtained by subtracting the baseline AoACS value from the follow-up AoACS value. The second assessment was performed from 2 years after the first determination. The non-progressors (63.2 ± 14.5 years) were significantly younger than the progressors (68.2 ± 10.8 years) (P = 0.0419). In addition, prescribed dose of 1α-hydroxy vitamin D₃ was significantly higher in the non-progressors (125.5 ± 109.1 μg) than progressors (84.8 ± 81.1 μg) (P = 0.0371). Multiple regression analysis revealed prescribed dose of 1α-hydroxy vitamin D₃ (β value = −0.324, P = 0.0051) as well as DBP (β value = −0.418, P = 0.007), serum levels of P (β value = 0.333, P = 0.006) and C-reactive protein (β value = 0.237, P = 0.0048) to be significant independent determinants of ΔAoACS. In conclusion, the evaluation of AoACS on chest radiography is a very simple tool in HD patients. Active vitamin D therapy seems to protect patients from developing vascular calcification.

Key words Aortic arch calcification · Chest radiography · Vitamin D · Hemodialysis · Cardiovascular disease

Introduction

Cardiovascular disease is the major cause of death in patients with chronic kidney disease (CKD).¹ Recently, vascular calcification in the coronary arteries and the aorta has been recognized as an important risk factor for cardiovascular disease in hemodialysis (HD) patients.² Vascular calcification is very common in end-stage renal disease (ESRD), especially in HD patients.³ The mechanisms of vascular calcification are hyperphosphatemia and elevated calcium (Ca) × phosphate (P) products.⁴⁻⁵ Vascular calcification induces stiffening of the vessel wall and reduces vascular compliance, which have been found to be predictive of cardiovascular mortality.⁶⁻⁸

Renal failure results in deficiency of active vitamin D₃ that attributes to impaired bone and mineral metabolism, cardiovascular complications, and suppressed immune functions. In fact, there are several reports showing that treatment with active vitamin D₃ improved these abnormalities.⁹⁻¹⁰ On the other hand, of concern is the possibility that treatment with vitamin D increases Ca × P products and may result in vascular calcification.¹¹ Although a previous study by Teng et al.¹² showed that survival rate was different between two groups of HD patients, one receiving calcitriol and the other receiving paricalcitol, a new vitamin D analogue having smaller effects on serum Ca and P, their study does not answer the question of whether to treat, or not to treat, with some forms of vitamin D in view of survival advantage in HD patients.

Thus, the benefit of treatment with active vitamin D in HD patients is not fully established. The aim of the present study was to examine the effects of oral 1α-hydroxy vitamin D₃ on the progression of aortic arch calcification (AoAC) estimated by chest radiography in HD patients.
Patients and methods

Study population

Out of 90 HD patients treated at the Dialysis Unit of Hidaka Hospital, 65 patients (40 men and 25 women) gave their informed consent to enroll this study. Twenty-five patients did not complete the study protocol from the start of HD for 2 years’ follow-up. Ten patients were transferred to the satellite clinic and 11 patients did not give their informed consent. Four patients were excluded from the study: 2 because of a past parathyroidec- tomy and 2 who were receiving pulse calcitriol therapy. The underlying diseases were type 2 diabetes mellitus (DM) in 26 patients (40%) and chronic glomerulonephritis without DM in 31, polycystic kidney disease in 4, nephrosclerosis in 3, and lupus nephritis in 1. Hemodialysis was performed three times weekly (4 h/day). The dialysis potassium concentration was 2.0 mEq/l and the calcium (Ca) concentration was 3.0 mEq/l. Based on the medications at entry, 48 patients were identified as regular vitamin D users and the remaining 17 patients as non-users. The principle of the prescription of vitamin D was to suppress serum intact parathyroid hormone (PTH) levels. Blood was drawn before starting each dialysis session after an overnight fast to measure the various markers, including Ca, P, albumin, hemoglobin, total cholesterol, high-density lipoprotein (HDL)-cholesterol, and triglyceride. Low-density lipoprotein (LDL)-cholesterol was calculated by the formula (total cholesterol – HDL cholesterol – triglyceride/5). The mean values of three measurements taken during the 3 months before chest radiology were used in the analysis. Blood pressure was recorded three times, after the subject had rested in the supine position for at least 10 min and the average value of the three measurements was adopted. Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg, or use of antihypertensive medication. Pulse pressure (PP) was calculated by the formula PP = SBP – DBP. Diabetes mellitus was defined by World Health Organization (WHO) criteria. Hyperlipidemia was defined as fasting serum total cholesterol ≥230 mg/dl, LDL-cholesterol ≥140 mg/dl, triglyceride ≥150 mg/dl, HDL-cholesterol <40 mg/dl, or use of lipid-lowering medication. Serum intact PTH was measured once at the time of chest radiology using an Allegro Intact PTH IRMA assay (Nichol’s Institute, San Juan Capistrano, CA, USA). The total prescribed doses of 1α-hydroxy vitamin D3 and CaCO3 during the follow-up period were calculated and used for statistical analyses. This study complies with the Declara- tion of Helsinki and in agreement with the guidelines approved by the ethics committee at our institution.

Evaluation of aortic arch calcification score (AoACS) by chest radiography

We performed a prospective assessment of all patients from the start of dialysis therapy from January 2004. Two radiologists (one specializing in chest radiography) indepen-